

STIC Search Report Biotech-Chem Library

STIC Database Tracking Number: 95235

TO: Shahnam J Sharareh Location: 2b19 / 3d13

W dnesday, June 04, 2003

Art Unit: 1617 Phone: 306-5400

Serial Number: 09 / 899629

From: Jan Delaval

Location: Biotech-Chem Library

CM1-1E07

Phone: 308-4498

jan.delaval@uspto.gov

Search Notes

Jan Delaval Reference Librarian Biotechnology & Chemical Library CM1 1E07 – 703-308-4498 jan.delaval@uspto.gov



=> fil req FILE 'REGISTRY' ENTERED AT 07:29:05 ON 04 JUN 2003 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2003 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 2 JUN 2003 HIGHEST RN 524673-75-4 DICTIONARY FILE UPDATES: HIGHEST RN 524673-75-4 2 JUN 2003

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d 145 sqide can tot

L45 ANSWER 1 OF 7 REGISTRY COPYRIGHT 2003 ACS

250614-40-5 REGISTRY RN

Indate (2-)-111In, [[5,5]-[N-[[4,7,10-tris](carboxy-.kappa.0)methyl]-CN 1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N10] acetyl]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-Dphenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE

SQL 10,5,5

multichain NTE

cyclic, cyclic

modified (modifications unspecified)

type	location		description	
bridge	Lys-5	- Lys-5'	covalent bridge, dimer	
stereo	Phe-4	-	D	
stereo	Phe-4'	-	D	

SEQ 1 RGDFK

HITS AT: 1-4, 5

SEQ 1 RGDFK

HITS AT: 1-4, 5

Jan Delavai Reference Librarian Biotechnology & Chemical Library CM1 1E07 - 703-308-4498 jan.delaval@uspto.gov

RELATED SEQUENCES AVAILABLE WITH SEQLINK

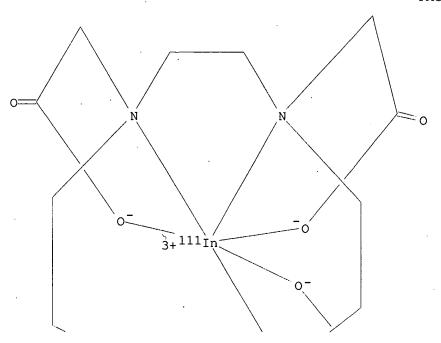
C75 H108 In N23 O23 . 2 H MF

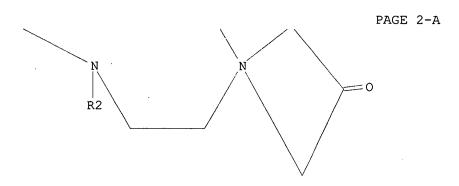
CI CCS

SR CA

CA, CAPLUS, TOXCENTER, USPATZ, USPATFULL LC STN Files:

PAGE 1-A





$$\begin{array}{c}
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/ \\
Ph-CH_2
\end{array}$$

R2

PAGE 4-A

●2 H⁺

5 REFERENCES IN FILE CA (1957 TO DATE) 5 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:255514

REFERENCE 2: 137:140780

REFERENCE 3: 137:109487

REFERENCE 4: 136:70083

REFERENCE 5: 131:351678

L45 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2003 ACS

RN 250614-39-2 REGISTRY

CN Lutetate(2-)-177Lu, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]-1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N10] acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE

SQL 10,5,5

NTE multichain

cyclic, cyclic

modified (modifications unspecified)

type	location		description	
bridge	Lys-5	- Lys-5'	covalent bridge,	dimer
stereo	Phe-4	-	D	
stereo	Phe-4'	-	D	

SEQ 1 RGDFK

HITS AT: 1-4, 5

SEQ 1 RGDFK

.

HITS AT: 1-4, 5

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C75 H108 Lu N23 O23 . 2 H

CI CCS

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPAT7, USPATFULL

PAGE 1-B

PAGE 2-A

●2 H+

6 REFERENCES IN FILE CA (1957 TO DATE) 6 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:255514

REFERENCE 2: 137:140780

REFERENCE 3: 137:109487

REFERENCE 4: 136:70083

REFERENCE 5: 135:177368

REFERENCE 6: 131:351678

L45 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2003 ACS

RN **250614-38-1** REGISTRY

CN Yttrate(2-)-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]-1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N10] acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

OTHER NAMES:

CN RP 697

FS PROTEIN SEQUENCE

SQL 10,5,5

NTE multichain

cyclic, cyclic

modified (modifications unspecified)

type	location		description	
bridge	Lys-5	- Lys-5'	covalent bridge,	dimer
stereo	Phe-4	-	D	
stereo	Phe-4'	-	D	

SEQ 1 RGDFK

SEQ 1 RGDFK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C75 H108 N23 O23 Y . 2 H

CI CCS

SR CA

LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, USPATZ, USPATFULL

PAGE 1-B

PAGE 2-A

8 REFERENCES IN FILE CA (1957 TO DATE)

8 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 138:255514 137:140780 REFERENCE 137:109487 REFERENCE

REFERENCE 136:123597

REFERENCE 136:70083

REFERENCE 135:185318

REFERENCE 135:177368

REFERENCE 8: 131:351678

L45 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2003 ACS

RN 250612-82-9 REGISTRY

Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), CN 5,5'-[N-[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethylethoxy-2-(1,1-dimethylethoxy)-2-oxoethylethoxy-2-(1,1-dimethylethoxy-2-(1,1tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 10,5,5

NTE multichain

cyclic, cyclic

modified (modifications unspecified)

type	loc	ation	description	
bridge	Lys-5	- Lys-5'	covalent bridge,	dimer
stereo	Phe-4	-	D	
stereo	Phe-4'	-	D	

1 RGDFK SEQ

HITS AT: 1-4, 5

SEQ 1 RGDFK

HITS AT: 1-4, 5

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C87 H137 N23 O23 . 2 C2 H F3 O2

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPAT7, USPATFULL

CM 1

CRN 250612-81-8

CMF C87 H137 N23 O23

PAGE 1-A

PAGE 2-A

| СH₂— СО₂H

CM 2

CRN 76-05-1 CMF C2 H F3 O2

F-C-CO₂H

6 REFERENCES IN FILE CA (1957 TO DATE)

6 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:255514

REFERENCE 2: 137:140780

REFERENCE 3: 137:109487

REFERENCE 4: 136:123597

REFERENCE 5: 136:70083

REFERENCE 6: 131:351678

L45 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2003 ACS

RN 250612-81-8 REGISTRY

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 10,5,5

NTE multichain

cyclic, cyclic

modified (modifications unspecified)

type	location		description		
bridge stereo stereo	Lys-5 Phe-4 Phe-4'	- Lys-5' - -	covalent D D	bridge,	dimer

SEQ 1 RGDFK

HITS AT: 1-4, 5

SEQ 1 RGDFK

HITS AT: 1-4, 5

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C87 H137 N23 O23

CI COM

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

PAGE 2-A

| Сн₂— со₂н

1 REFERENCES IN FILE CA (1957 TO DATE)

1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 135:177368

L45 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2003 ACS

RN 250612-07-8 REGISTRY

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 10,5,5

NTE multichain

cyclic, cyclic

modified (modifications unspecified)

type	loca	tion	description
bridge	Lys-5	- Lys-5'	covalent bridge, dimer
stereo	Phe-4		D
stereo	Phe-4'		D

SEQ 1 RGDFK

HITS AT: 1-4, 5

SEQ 1 RGDFK

HITS AT: 1-4, 5

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C75 H113 N23 O23 . 2 C2 H F3 O2

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

CM 1

CRN 250612-06-7

CMF C75 H113 N23 O23

PAGE 1-A

PAGE 1-B

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CM 2
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CRN 76-05-1 CMF C2 H F3 O2

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F-C-CO<sub>2</sub>H
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6 REFERENCES IN FILE CA (1957 TO DATE)

6 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:255514

REFERENCE 2: 137:140780

REFERENCE 3: 137:109487

REFERENCE 4: 136:123597

REFERENCE 5: 136:70083

REFERENCE 6: 131:351678

L45 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2003 ACS

RN **250612-06-7** REGISTRY

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN SU 015

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 10,5,5

NTE multichain

cyclic, cyclic

modified (modifications unspecified)

type	location		description	
bridge	Lys-5	- Lys-5'	covalent bridge, dimer	
stereo	Phe-4		D	
stereo	Phe-4'	-	D	

SEQ 1 RGDFK

HITS AT: 1-4, 5

SEQ 1 RGDFK

HITS AT: 1-4, 5

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C75 H113 N23 O23

CI ·COM

SR CA

LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, USPAT7ULL

5 REFERENCES IN FILE CA (1957 TO DATE)

5 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:255514

REFERENCE 2: 136:70083

REFERENCE 3: 135:185318

REFERENCE 4: 135:177368

REFERENCE 5: 131:351678

=> fil uspatall

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CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)
FILE 'USPAT2' ENTERED AT 07:29:35 ON 04 JUN 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)
=> d 152 bib abs hitstr tot
L52
     ANSWER 1 OF 14 USPATFULL
ΑN
       2003:123076 USPATFULL
TΤ
       Vitronectin receptor antagonist pharmaceuticals
       Cheesman, Edward H., Lunenberg, MA, United States
TN
       Sworin, Michael, Tyngsboro, MA, United States
       Rajopadhye, Milind, Westford, MA, United States
       Bristol-Myers Squibb Pharma Company, Princeton, NJ, United States (U.S.
PΑ
       corporation)
PΙ
       US 6558649
                               20030506
AΙ
       US 1999-466582
                                19991217 (9)
PRAI
       US 1998-112831P
                           19981218 (60)
DT
       Utility
FS
       GRANTED
EXNAM
       Primary Examiner: Jones, Dameron L.
LREP
       Woodcock Washburn LLP
CLMN
       Number of Claims: 9
ECL
       Exemplary Claim: 1
DRWN
       0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 4950
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB
       The present invention describes novel compounds of the formula:
```

(Q).sub.d--L.sub.n--C.sub.h,

useful for the diagnosis and treatment of cancer, methods of imaging tumors in a patient, and methods of treating cancer in a patient. The present invention also provides novel compounds useful for monitoring therapeutic angiogenesis treatment and destruction of new angiogenic vasculature. The present invention further provides novel compounds useful for imaging atherosclerosis, restenosis, cardiac ischemia and myocardial reperfusion injury. The present invention still further provides novel compounds useful for the treatment of rheumatoid arthritis. The pharmaceuticals are comprised of a targeting moiety that binds to a receptor that is upregulated during angiogenesis, an optional linking group, and a therapeutically effective radioisotope or diagnostically effective imageable moiety. The imageable moiety is a gamma ray or positron emitting radioisotope, a magnetic resonance imaging contrast agent, an X-ray contrast agent, or an ultrasound contrast agent.

CRN 250612-81-8 CMF C87 H137 N23 O23

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PAGE 1-B

PAGE 2-A

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250612-06-7P 250612-07-8P

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250612-06-7 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis- (9CI) (CA INDEX NAME)

PAGE 1-A

RN 250612-07-8 USPATFULL
CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-06-7 CMF C75 H113 N23 O23

PAGE 1-A

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250614-38-1P 250614-39-2P 250614-40-5P

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250614-38-1 USPATFULL

PAGE 1-A

PAGE 1-B

PAGE 2-A

RN 250614-39-2 USPATFULL

CN Lutetate(2-)-177Lu, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-B

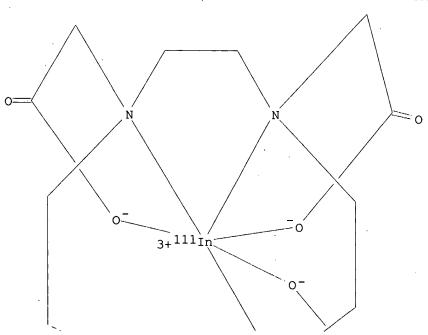
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●2 µ+

RN 250614-40-5 USPATFULL

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0]acetyl]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-Dphenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-A



$$^{\rm R}$$
 / Ph-CH2

R2

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 4-A

2 H+

L52 ANSWER 2 OF 14 USPATFULL AN 2003:102466 USPATFULL

TI Benzodiazepine vitronectin receptor antagonist pharmaceuticals

IN Cheesman, Edward H, Lunenberg, MA, United States

```
Sworin, Michael, Tyngsboro, MA, United States
PA
       Bristol-Myers Squibb Pharma Company, Princeton, NJ, United States (U.S.
       corporation)
PΙ
       US 6548663
                                20030415
                          В1
AΙ
       US 1999-281050
                                19990330 (9)
                           19981218 (60)
PRAI
       US 1998-112715P
                           19981218 (60)
       US 1998-112829P
       US 1998-112732P
                           19981218 (60)
       US 1998-112831P
                           19981218 (60)
       US 1998-80150P
                           19980331 (60)
DT
       Utility
FS
       GRANTED
EXNAM
       Primary Examiner: Raymond, Richard L.; Assistant Examiner:
       Balasubramanian, Venkataraman
LREP
       Woodcock Washburn LLP
CLMN
       Number of Claims: 4
ECL
       Exemplary Claim: 1
DRWN
       0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 4239
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB
       The present invention describes novel compounds of the formula:
       (Q).sub.d--L.sub.n--C.sub.h,
       useful for the diagnosis and treatment of cancer, methods of imaging
       tumors in a patient, and methods of treating cancer in a patient. The
       present invention also provides novel compounds useful for monitoring
       therapeutic angiogenesis treatment and destruction of new angiogenic
       vasculature. The pharmaceuticals are comprised of a targeting moiety
       that binds to a receptor that is upregulated during angiogenesis, an
```

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

```
IT 250612-82-9P
```

(prepn. of peptide derivs. for the imaging of angiogenic disorders) 250612-82-9 USPATFULL

optional linking group, and a therapeutically effective radioisotope or diagnostically effective imageable moiety. The imageable moiety is a gamma ray or positron emitting radioisotope, a magnetic resonance imaging contrast agent, an X-ray contrast agent, or an ultrasound

RN 250612-82-9 USPATFULL
CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate)
(9CI) (CA INDEX NAME)

CM 1

CRN 250612-81-8 CMF C87 H137 N23 O23

contrast agent.

PAGE 1-A

PAGE 1-B

Сн2-со2н

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250612-06-7P 250612-07-8P

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250612-06-7 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis- (9CI) (CA INDEX NAME)

PAGE 1-A

RN 250612-07-8 USPATFULL

CN Cyclo(L-arginylglycyl-L-alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-06-7 CMF C75 H113 N23 O23

PAGE 1-A

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250614-38-1P 250614-39-2P 250614-40-5P

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250614-38-1 USPATFULL

PAGE 2-A

RN 250614-39-2 USPATFULL

CN Lutetate(2-)-177Lu, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-B

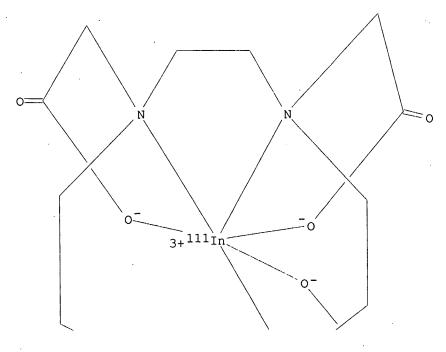
PAGE 2-A

●2 H+

RN 250614-40-5 USPATFULL CN Indate(2-)-111In, [[5,

Indate(2-)-111In, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl] 1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
 0]acetyl]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-A



$$^{\rm R}_{/}$$
 Ph-CH2

R2

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 4-A

2 H+

L52 ANSWER 3 OF 14 USPATFULL

AN 2003:81434 USPATFULL

ΤI

Pharmaceuticals for the imaging of angiogenic disorders

IN Rajopadhye, Milind, Westford, MA, United States

Edwards, D. Scott, Burlington, MA, United States Barrett, John A., Groton, MA, United States Carpenter, Jr., Alan P., Carlisle, MA, United States Harris, Thomas D., Samel, NH, United States Heminway, Stuart J., Lowell, MA, United States Liu, Shuang, Chelmsford, MA, United States Singh, Prahlad R., Arlington, MA, United States PΑ Bristol-Myers Squibb Pharma Company, Princeton, NJ, United States (U.S. corporation) PΙ US 6537520 В1 20030325. AΙ US 2000-599295 20000621 (9) RLI Continuation-in-part of Ser. No. US 1999-281474, filed on 30 Mar 1999 19981218 (60) PRAI US 1998-112715P 19980331 (60) US 1998-80150P DΤ Utility FS GRANTED EXNAM Primary Examiner: Jones, Dameron L. LREP Golian, Paul D. CLMN Number of Claims: 37 ECL Exemplary Claim: 1 DRWN 0 Drawing Figure(s); 0 Drawing Page(s) LN.CNT 6846 CAS INDEXING IS AVAILABLE FOR THIS PATENT. AΒ The present invention describes novel compounds of the formula:

(Q).sub.d--L.sub.n--C.sub.h,

useful for the diagnosis and treatment of cancer, methods of imaging tumors in a patient, and methods of treating cancer in a patient. The present invention also provides novel compounds useful for monitoring therapeutic angiogenesis treatment and destruction of new angiogenic vasculature. The pharmaceuticals are comprised of a targeting moiety that binds to a receptor that is upregulated during angiogenesis, an optional linking group, and a therapeutically effective radioisotope or diagnostically effective imageable moiety. The imageable moiety is a gamma ray or positron emitting radioisotope, a magnetic resonance imaging contrast agent, an X-ray contrast agent, or an ultrasound contrast agent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 250612-06-7P 250612-07-8P

(prepn. of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

RN 250612-06-7 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

RN 250612-07-8 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-06-7 CMF C75 H113 N23 O23

PAGE 1-A

PAGE 1-B

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250614-38-1P 250614-39-2P 250614-40-5P

(prepn. of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

RN 250614-38-1 USPATFULL

CN Yttrate(2-)-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA·INDEX NAME)

PAGE 1-B

PAGE 2-A

●2 H⁺

RN 250614-39-2 USPATFULL

CN Lutetate(2-)-177Lu, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-B

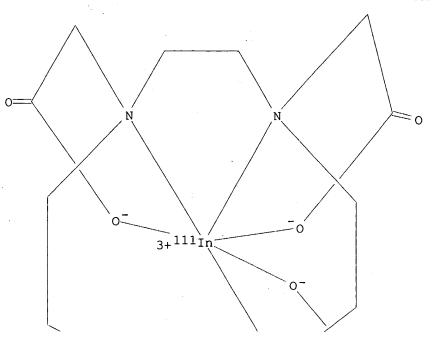
PAGE 2-A

●2 H+

RN 250614-40-5 USPATFULL

CN Indate(2-)-111In, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]-1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1 0]acetyl]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)





PAGE 2-A

R2

PAGE 4-A

●2 H⁺

IT 250612-82-9P

(prepn. of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

RN 250612-82-9 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-81-8 CMF C87 H137 N23 O23

PAGE 1-A

PAGE 1-B

Сн2-со2н

PAGE 2-A

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 10098-91-6, y90, biological studies

(radioisotope for use with peptide derivs. for the treatment of cancer in combination therapy)

RN 10098-91-6 USPATFULL

CN Yttrium, isotope of mass 90 (8CI, 9CI) (CA INDEX NAME)

90_Y

```
ANSWER 4 OF 14 USPATFULL
L52
ΑN
       2002:321986 USPATFULL
ΤI
       VITRONECTIN RECEPTOR ANTAGONIST PHARMACEUTICALS
IN
       HARRIS, THOMAS D., SALEM, NH, UNITED STATES
       RAJOPADHYE, MILIND, WESTFORD, MA, UNITED STATES
PΙ
       US 2002182147
                         Α1
                               20021205
       US 6511648
                          B2
                               20030128
       US 1999-465300
                          Α1
                               19991217 (9)
ΑI
PRAI
       US 1998-112732P
                           19981218 (60)
DT
       Utility
FS
       APPLICATION
LREP
       BRISTOL-MYERS SQUIBB PHARMA COMPANY, PATENT DEPARTMENT, P.O. BOX 4000,
       PRINCETON, NJ, 08543-4000
CLMN
       Number of Claims: 57
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 7362
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AΒ
       The present invention describes novel compounds of the formula:
```

(Q).sub.d--L.sub.n--C.sub.h,

useful for the diagnosis and treatment of cancer, methods of imaging tumors in a patient, and methods of treating cancer in a patient. The present invention also provides novel compounds useful for monitoring therapeutic angiogenesis treatment and destruction of new angiogenic vasculature. The present invention further provides novel compounds useful for imaging atherosclerosis, restenosis, cardiac ischemia, and myocardial reperfusion injury. The present invention still further provides novel compounds useful for the treatment of rheumatoid arthritis. The pharmaceuticals are comprised of a targeting moiety that binds to a receptor that is upregulated during angiogenesis, an optional linking group, and a therapeutically effective radioisotope or diagnostically effective imageable moiety. The imageable moiety is a gamma ray or positron emitting radioisotope, a magnetic resonance imaging contrast agent, an X-ray contrast agent, or an ultrasound contrast agent.

IT 250612-82-9P

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250612-82-9 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate)
(9CI) (CA INDEX NAME)

CM 1

CRN 250612-81-8 CMF .C87 H137 N23 O23

PAGE 1-A

PAGE 1-B

PAGE 2-A

CH2-CO2H

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250612-06-7P 250612-07-8P

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250612-06-7 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis- (9CI) (CA INDEX NAME)

HO2C-CH2

PAGE 1-A

PAGE 1-B

RN 250612-07-8 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1 .

CRN 250612-06-7 CMF C75 H113 N23 O23 HO₂C-CH₂

PAGE 1-B

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250614-38-1P 250614-39-2P 250614-40-5P

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250614-38-1 USPATFULL

CN Yttrate(2-)-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-B

PAGE 2-A

2 H+

RN

250614-39-2 USPATFULL Lutetate(2-)-177Lu, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]-CN 1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1 0]acetyl-.kappa.0]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

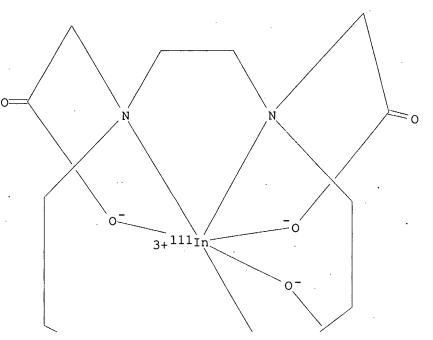
PAGE 2-A

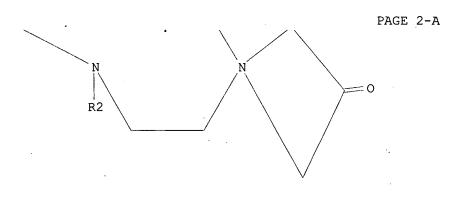
●2 H+

RN 250614-40-5 USPATFULL

CN Indate(2-)-111In, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-Dphenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-A





$$Ph-CH_2$$

R2

PAGE 4-A

●2 H

L52 ANSWER 5 OF 14 USPATFULL

AN 2002:227617 USPATFULL

TI Stable radiopharmaceutical compositions and methods for preparation thereof

IN Liu, Shuang, Chelmsford, MA, UNITED STATES

Barrett, John A., Groton, MA, UNITED STATES

Carpenter, Alan P., JR., Carlisle, MA, UNITED STATES

PI US 2002122768 A1 20020905

AI US 2001-899629. A1 20010705 (9)

PRAI US 2000-216396P 20000706 (60)

DT Utility

FS APPLICATION

LREP BRISTOL-MYERS SQUIBB PHARMA COMPANY, PATENT DEPARTMENT, P.O. BOX 4000, PRINCETON, NJ, 08543-4000

MNI Namber of Claims 00

CLMN Number of Claims: 92

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 4115

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention provides stable radiopharmaceutical compositions including a therapeutic radionuclide and an effective stabilizing amount of an aromatic stabilizer (e.g., a polyhydroxylated aromatic compound, an aromatic amine, or a hydroxylated aromatic amine), alone or in combination with other antioxidants or stabilizers, to inhibit radiolytic degradation of radiopharmaceuticals. The present invention also provides improved radiopharmaceutical formulations by the use of an aromatic stabilizing agent (e.g., a polyhydroxylated aromatic compound, an aromatic amines, or a hydroxylated aromatic amine), and/or low temperature storage. The present invention also provides processes for making stable radiopharmaceutical compositions. The present invention also provides the use of the pharmaceutical compositions in medical therapy and/or medical diagnosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 250612-82-9P

(prepn. of chelator-optional linker-biomol. conjugates for use in stable radiopharmaceutical compns.)

RN 250612-82-9 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA.INDEX NAME)

CM 1

CRN 250612-81-8 CMF C87 H137 N23 O23

PAGE 1-A

PAGE 1-B

PAGE 2-A

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250612-07-8P

(prepn. of chelator-optional linker-biomol. conjugates for use in stable radiopharmaceutical compns.)

RN 250612-07-8 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-06-7 CMF C75 H113 N23 O23

PAGE 1-A

PAGE 1-B

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250614-38-1P

(prepn. of stable radiopharmaceutical compns. useful for tumor therapy)

RN 250614-38-1 USPATFULL

CN Yttrate(2-)-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-B

PAGE 2-A

●2 H+

IT 10098-91-6D, 90Y, complexes, biological studies (prepn. of stable radiopharmaceutical compns. useful for tumor therapy)

RN 10098-91-6 USPATFULL

CN Yttrium, isotope of mass 90 (8CI, 9CI) (CA INDEX NAME)

90_Y

IT 490-79-9, Gentisic acid

(stabilizing agent; prepn. of stable radiopharmaceutical compns. useful for tumor therapy)

RN 490-79-9 USPATFULL

CN Benzoic acid, 2,5-dihydroxy- (9CI) (CA INDEX NAME)

L52 ANSWER 6 OF 14 USPATFULL

AN 2002:198232 USPATFULL

TI Simultaneous imaging of cardiac perfusion and a vitronectin receptor

targeted imaging agent

IN Carpenter,, Alan P., JR., Carlisle, MA, UNITED STATES

PI US 2002106325 A1 20020808

AI US 2001-995388 A1 20011127 (9)

PRAI PH 2000-7201 20001127

DT Utility

FS APPLICATION

LREP BRISTOL-MYERS SQUIBB PHARMA COMPANY, PATENT DEPARTMENT, P.O. BOX 4000,

PRINCETON, NJ, 08543-4000

CLMN Number of Claims: 66

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 6224

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention describes a method of concurrent imaging in a AΒ mammal comprising:

- a) administering to said mammal a vitronectin receptor targeted imaging agent and a perfusion imaging agent; and
- b) concurrently detecting the vitronectin target imaging agent bound at the vitronectin receptor and the perfusion imaging agent; and
- c) forming an image from the detection of said vitronectin receptor targeted imaging agent and said perfusion imaging agent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 250612-07-8P

(prepn. of peptides and simultaneous imaging of cardiac perfusion and a vitronectin receptor targeted imaging agent)

250612-07-8 USPATFULL RN

Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), CN 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-06-7 C75 H113 N23 O23 CMF

PAGE 1-A

PAGE 1-B

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250614-38-1P 250614-39-2P 250614-40-5P

(prepn. of peptides and simultaneous imaging of cardiac perfusion and a vitronectin receptor targeted imaging agent)

RN 250614-38-1 USPATFULL

CN Yttrate(2-)-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

PAGE 2-A

RN 250614-39-2 USPATFULL

CN Lutetate(2-)-177Lu, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-B

PAGE 2-A

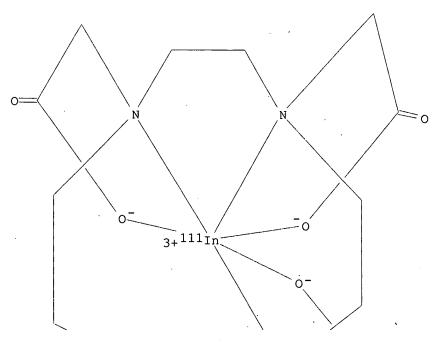
●2 H+

RN 250614-40-5 USPATFULL

CN

Indate(2-)-111In, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl] 1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
 0]acetyl]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-A



R2

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 4-A

2 H+

IT 250612-82-9P

(prepn. of peptides and simultaneous imaging of cardiac perfusion and a vitronectin receptor targeted imaging agent)

RN 250612-82-9 USPATFULL

 ${\tt CN} \qquad {\tt Cyclo}\left({\tt L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl}\right),$

5,5'-[N-[[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-81-8 CMF C87 H137 N23 O23

PAGE 1-A

PAGE 1-B

PAGE 2-A

| Сн₂- со₂н

CM 2

CRN 76-05-1 CMF C2 H F3 O2

L52 ANSWER 7 OF 14 USPATFULL

F-C-CO₂H

```
ΑN
       2002:135936 USPATFULL
TI
       Arrayable thermal assays
IN
       Ludington, David Norman, Newton, PA, United States
       Fare, Thomas Louis, Redmond, WA, United States
       Lo Iacono, Dominic Joseph, Yardville, NJ, United States
       Davis, Timothy James, Columbus, NJ, United States
       Semus, Helen Jiang, Bensalem, PA, United States
       Stabile, Paul John, Langhorne, PA, United States
       Guarnieri, Frank, Brooklyn, NY, United States
       Granzow, Russell Todd, Titusville, NJ, United States
       Zanzucchi, Peter J., Lawrenceville, NJ, United States
       Chiang, William, Monmouth Jct., NJ, United States
PA
       Sarnoff Corporation, Princeton, NJ, United States (U.S. corporation)
PΙ
       US 6402369
                          В1
                               20020611
AΙ
       US 1999-432736
                               19991102 (9)
                           19981216 (60)
PRAI
       US 1998-112629P
       US 1998-106811P
                           19981103 (60)
DT
       Utility
FS
       GRANTED
EXNAM
       Primary Examiner: Gutierrez, Diego; Assistant Examiner: Pruchnic, Jr.,
       Stanley J.
LREP
       Burke, William J.
       Number of Claims: 16
CLMN
ECL
       Exemplary Claim: 1
       11 Drawing Figure(s); 4 Drawing Page(s)
DRWN
LN.CNT 1360
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Provided are, among other things, devices for and methods for performing
       thermal signature assays on a two or more samples in an array, using
       active/control base thermopiles, the method comprising: [a] performing a
       heat transfer to the two or more samples in each of a two or more
       containers, using at least one base thermopile in thermal communication
       with the two or more containers; and [b] determining a total heat
       transferred to the samples by the base thermopile in step [a]; and [c]
       sensing in real time a temperature difference between a first sample and
       a second sample of the two or more samples resulting from performing
       step [a].
```

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 250612-82-9P

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250612-82-9 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate)
(9CI) (CA INDEX NAME)

CM 1

CRN 250612-81-8 CMF C87 H137 N23 O23

PAGE 1-A

PAGE 1-B

PAGE 2-A

| Сн₂— со₂н

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250612-06-7P 250612-07-8P

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250612-06-7 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

RN 250612-07-8 USPATFULL
CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-06-7 CMF C75 H113 N23 O23

PAGE 1-A

PAGE 1-B

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250614-38-1P 250614-39-2P 250614-40-5P

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250614-38-1 USPATFULL

CN Yttrate(2-)-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-B

PAGE 2-A

●2 H+

RN 250614-39-2 USPATFULL

CN Lutetate(2-)-177Lu, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

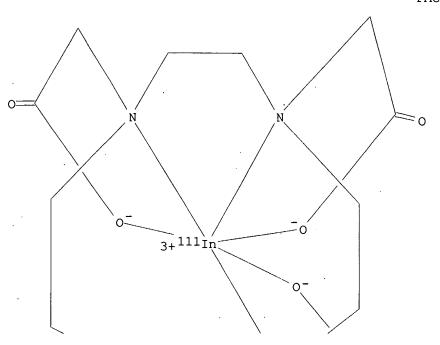
PAGE 2-A

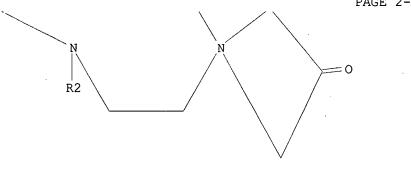
●2 H+

RN 250614-40-5 USPATFULL

CN Indate(2-)-111In, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]-1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1 0]acetyl]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-A





PAGE 4-A

●2 H+

```
T<sub>1</sub>52
    ANSWER 8 OF 14 USPATFULL
       2002:119921 USPATFULL
AN
TT
       Vitronectin receptor antagonist pharmaceuticals
IN
       Harris, Thomas D., Salem, NH, UNITED STATES
       Rajopadhye, Milind, Westford, MA, UNITED STATES
PΙ
       US 2002061909
                           Α1
                                20020523
ΑI
       US 2001-948390
                           A1
                                20010907 (9)
RLI
       Continuation of Ser. No. US 1999-465300, filed on 17 Dec 1999, PENDING
PRAI
       US 1998-112732P
                            19981218 (60)
DT
       Utility
FS
       APPLICATION
LREP
       DuPont Pharmaceuticals Company, c/o E. I. duPont de Nemours and Company,
       Legal - Patents, 1007 Market Street, Wilmington, DE, 19898
CLMN
       Number of Claims: 57
ECI.
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 7403
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AΒ
       The present invention describes novel compounds of the formula:
```

(Q).sub.d--L.sub.n--C.sub.h,

useful for the diagnosis and treatment of cancer, methods of imaging tumors in a patient, and methods of treating cancer in a patient. The present invention also provides novel compounds useful for monitoring therapeutic angiogenesis treatment and destruction of new angiogenic vasculature. The present invention further provides novel compounds useful for imaging atherosclerosis, restenosis, cardiac ischemia, and myocardial reperfusion injury. The present invention still further provides novel compounds useful for the treatment of rheumatoid arthritis. The pharmaceuticals are comprised of a targeting moiety that binds to a receptor that is upregulated during angiogenesis, an optional linking group, and a therapeutically effective radioisotope or diagnostically effective imageable moiety. The imageable moiety is a gamma ray or positron emitting radioisotope, a magnetic resonance imaging contrast agent, an X-ray contrast agent, or an ultrasound contrast agent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 250612-82-9P

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250612-82-9 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-81-8 CMF C87 H137 N23 O23

PAGE 1-A

PAGE 2-A

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250612-06-7P 250612-07-8P

(prepn. of peptide derivs. for the imaging of angiogenic disorders) 250612-06-7 USPATFULL

RN 250612-06-7 USPATFULL
CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

RN 250612-07-8 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-06-7 CMF C75 H113 N23 O23

PAGE 1-A

PAGE 1-B

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250614-38-1P 250614-39-2P 250614-40-5P

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250614-38-1 USPATFULL

CN Yttrate(2-)-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-B

PAGE 2-A

●2 H+

RN 250614-39-2 USPATFULL

CN Lutetate(2-)-177Lu, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 2-A

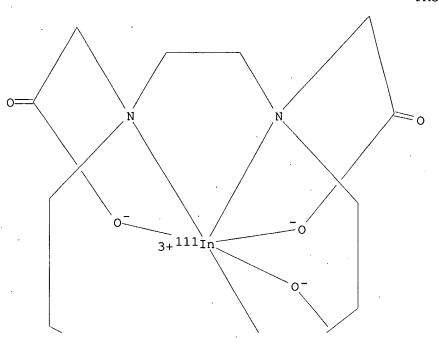
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 NH_2
 R_2
 NH

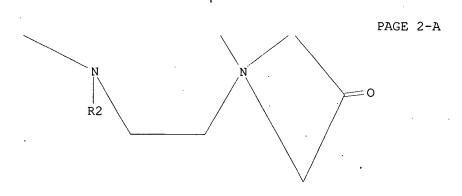
●2 H+

RN 250614-40-5 USPATFULL

CN Indate(2-)-111In, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-Dphenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-A





R2

PAGE 4-A

●2 H+

```
L52
    ANSWER 9 OF 14 USPATFULL
ΑN
       2002:26835 USPATFULL
TI
       QUINOLONE VITRONECTIN RECEPTOR ANTAGONIST PHARMACEUTICALS
IN
       HARRIS, THOMAS DAVID, SALEM, NH, UNITED STATES
PΙ
       US 2002015680
                          Α1
                                20020207
       US 6524553
                           В2
                                20030225
ΑI
       US 1999-281209
                          Α1
                                19990330 (9)
PRAI
       US 1998-80150P
                            19980331 (60)
       US 1998-112715P
                            19981218 (60)
       US 1998-112829P
                            19981218 (60)
       US 1998-112732P
                            19981218 (60)
       US 1998-112831P
                            19981218 (60)
DT
       Utility
FS
       APPLICATION
LREP
       Dupont Pharmaceuticals Company, Legal Department - Patents, 1007 Market
       Street, Wilmington, DE, 19898
CLMN
       Number of Claims: 48
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 6696
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AΒ
       The present invention describes novel compounds of the formula:
```

(Q).sub.d--L.sub.n--C.sub.h,

useful for the diagnosis and treatment of cancer, methods of imaging tumors in a patient, and methods of treating cancer in a patient. The present invention also provides novel compounds useful for monitoring therapeutic angiogenesis treatment and destruction of new angiogenic vasculature. The pharmaceuticals are comprised of a targeting moiety that binds to a receptor that is upregulated during angiogenesis, an optional linking group, and a therapeutically effective radioisotope or diagnostically effective imageable moiety. The imageable moiety is a gamma ray or positron emitting radioisotope, a magnetic resonance imaging contrast agent, an X-ray contrast agent, or an ultrasound contrast agent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 250612-82-9P

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250612-82-9 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate)
(9CI) (CA INDEX NAME)

CM 1

CRN 250612-81-8 CMF C87 H137 N23 O23

PAGE 1-A

PAGE 2-A

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250612-06-7P 250612-07-8P

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250612-06-7 USPATFULL CN Cyclo(L-arginylglycyl-I

Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis- (9CI) (CA INDEX NAME)

HO2C-CH2

PAGE 1-B

RN 250612-07-8 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-06-7 CMF C75 H113 N23 O23

PAGE 1-A

PAGE 1-B

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250614-38-1P 250614-39-2P 250614-40-5P

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250614-38-1 USPATFULL

CN Yttrate(2-)-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-B

PAGE 2-A

●2 H+

RN. 250614-39-2 USPATFULL

CN Lutetate(2-)-177Lu, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]-1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1 0]acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

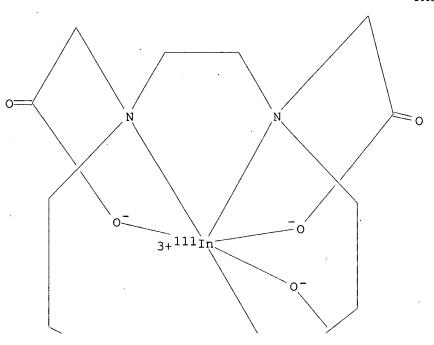
PAGE 2-A

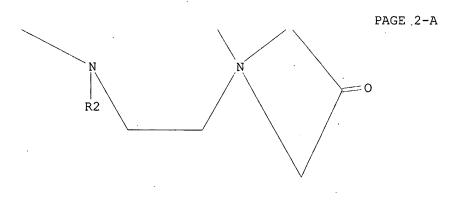
●2 H+

RN 250614-40-5 USPATFULL

CN Indate(2-)-111In, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-Dphenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-A





R2

PAGE 4-A

●2 H+

```
L52
     ANSWER 10 OF 14 USPATFULL
AN
       2002:3593 USPATFULL
TΤ
       PHARMACEUTICALS FOR THE IMAGING OF ANGIOGENIC DISORDERS
IN
       RAJOPADHYE, MILIND, WESTFORD, MA, UNITED STATES
       EDWARDS, D. SCOTT, BURLINGTON, MA, UNITED STATES
       HARRIS, THOMAS D., SAMEL, NH, UNITED STATES
       HAMINWAY, STUART J., LOWELL, MA, UNITED STATES
         LIU, SHUANG, CHELMSFORD, MA, UNITED STATES
       SINGH, PRAHLAD R., ARLINGTON, MA, UNITED STATES
PΙ
       US 2002001566
                          A1
                                20020103
AΙ
       US 1999-281474
                          A1
                                19990330 (9)
       US 1998-80150P
PRAI
                           19980331 (60)
       US 1998-112715P
                           19981218 (60)
DT
       Utility
FS
       APPLICATION
LREP
       DAVID H. VANCE, DUPONT PHARMACEUTICALS COMPANY, C/O E. I. DU PONT DE
       NEMOURS AND CO., LEGAL - PATENTS-1007 MARKET STREET, WILMINGTON, DE,
       19898
CLMN
       Number of Claims: 51
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 5872
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ÀΒ
       The present invention describes novel compounds of the formula:
```

(Q).sub.d--L.sub.n--C.sub.h,

useful for the diagnosis and treatment of cancer, methods of imaging tumors in a patient, and methods of treating cancer in a patient. The present invention also provides novel compounds useful for monitoring therapeutic angiogenesis treatment and destruction of new angiogenic vasculature. The pharmaceuticals are comprised of a targeting moiety that binds to a receptor that is upregulated during angiogenesis, an optional linking group, and a therapeutically effective radioisotope or diagnostically effective imageable moiety. The imageable moiety is a gamma ray or positron emitting radioisotope, a magnetic resonance imaging contrast agent, an X-ray contrast agent, or an ultrasound

contrast agent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 250612-82-9P

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250612-82-9 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-81-8

CMF C87 H137 N23 O23

PAGE 1-A

PAGE 2-A

| Сн₂— со₂н

CM 2

CRN 76-05-1 CMF C2 H F3 O2

F-C-CO₂H

IT 250612-06-7P 250612-07-8P

(prepn. of peptide derivs. for the imaging of angiogenic disorders) RN $\,$ 250612-06-7 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

RN 250612-07-8 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-06-7 CMF C75 H113 N23 O23

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250614-38-1P 250614-39-2P 250614-40-5P

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250614-38-1 USPATFULL

CN Yttrate(2-)-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-B

PAGE 2-A

$$(CH_2)$$
 $\stackrel{H}{3}$ NH_2 NH

●2 H+

RN 250614-39-2 USPATFULL

CN Lutetate(2-)-177Lu, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]-1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1 0]acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

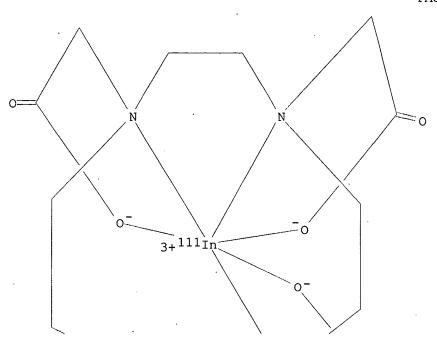
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R2 NH

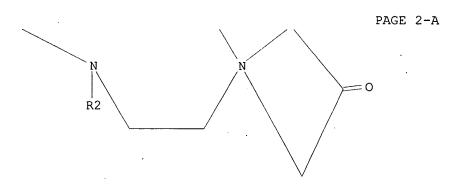
●2 H+

RN 250614-40-5 USPATFULL

CN Indate(2-)-111In, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-Dphenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-A





R2

PAGE 4-A

●2 H+

```
ANSWER 11 OF 14 USPATFULL
L52
AN
       2001:214639 USPATFULL
TΙ
       Indazole vitronectin receptor antagonist pharmaceuticals
       Rajopadhye, Milind, Westford, MA, United States
ΙN
       Harris, Thomas David, Salem, NH, United States
PA
       DuPont Pharmaceuticals Company, Wilmington, DE, United States (U.S.
       corporation)
ΡI
       US 6322770
                           В1
                                20011127
ΑI
       US 1999-281207
                                19990330 (9)
DT
       Utility
FS
       GRANTED
       Primary Examiner: Jones, Dameron L.
EXNAM
LREP
       Dolan, Peter L.
       Number of Claims: 70
CLMN
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 6228
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AΒ
       The present invention d ribs novel compounds of the formula:
```

(Q).sub.d --L.sub.n --C.sub.h,

useful for the diagnosis and treatment of cancer, methods of imaging tumors in a patient, and methods of treating cancer in a patient. The present invention also provides novel compounds useful for monitoring therapeutic angiogenesis treatment and destruction of new angiogenic vasculature. The pharmaceuticals are comprised of a targeting moiety that binds to a receptor that is upregulated during angiogenesis, an optional linking group, and a therapeutically effective radioisotope or diagnostically effective imageable moiety. The imageable moiety is a gamma ray or positron emitting radioisotope, a magnetic resonance imaging contrast agent, an X-ray contrast agent, or an ultrasound contrast agent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 250612-82-9P

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250612-82-9 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-81-8 CMF C87 H137 N23 O23

PAGE 1-A

PAGE 2-A

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250612-06-7P 250612-07-8P

(prepn. of peptide derivs. for the imaging of angiogenic disorders) 250612-06-7 USPATFULL

RN 250612-06-7 USPATFULL CN Cyclo(L-arginylglycyl-

Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1yl]acetyl]-L-glutamoyl]bis- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

RN 250612-07-8 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-06-7 CMF C75 H113 N23 O23 ${\tt HO_2C-CH_2}$

PAGE 1-A

PAGE 1-B

CM 2

CRN 76-05-1 CME C2 H F3 O2

IT 250614-38-1P 250614-39-2P 250614-40-5P

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250614-38-1 USPATFULL

CN Yttrate(2-)-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-B

PAGE 2-A

●2 H+

RN 250614-39-2 USPATFULL

CN Lutetate(2-)-177Lu, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]-1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1 0]acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

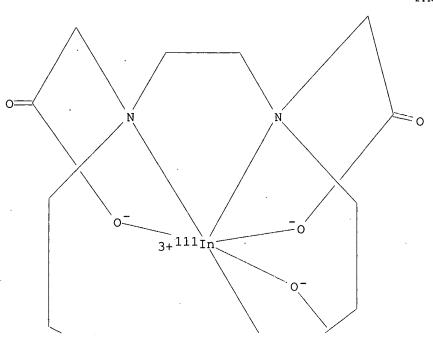
PAGE 2-A

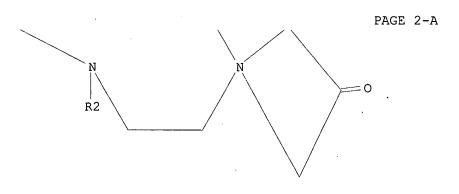
●2 H+

RN 250614-40-5 USPATFULL

CN Indate(2-)-111In, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-Dphenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-A





R2

PAGE 4-A

●2 H⁻

```
L52
    ANSWER 12 OF 14 USPATFULL
       2001:133415 USPATFULL
ΑN
ΤI
       DRIVING VOLTAGE GENERATOR OF LIQUID CRYSTAL DISPLAY UNIT
IN
       KAKUTA, RYOHEI, FUKUSHIMA-KEN, Japan
       NAGAKUBO, HIDEAKI, FUKUSHIMA-KEN, Japan
       TOKITA, SEIJI, FUKUSHIMA-KEN, Japan
       YAMAZAKI, MITSUAKI, FUKUSHIMA-KEN, Japan
PΙ
       US 2001013864
                          Α1
                                20010816
ΑI
       US 1998-112715
                          Α1
                                19980709 (9)
PRAI
       JP 1997-184190
                           19970709
DT
       Utility
FS
       APPLICATION
LREP
       BRINKS HOFER GILSON & LIONE, P.O. BOX 10395, CHICAGO, IL, 60610
CLMN
       Number of Claims: 10
ECL
       Exemplary Claim: 1
DRWN
       4 Drawing Page(s)
LN.CNT 338
```

(of a liquid crystal display unit) which can easily adjust output voltages. In this driving voltage generator, a DC-DC converter raises an input voltage (5 [V]) and produces voltages VH and VL. Resistors divide a voltage difference between the voltages VH and VL with resistors. Operational amplifiers output through current amplification each voltage divided by resistance. In the present invention, the external size can be reduced because only two output terminals are required for the DC-DC converter. In addition, manufacturing cost can be lowered because only

There is provided a small size and low price driving voltage generator

converter. In addition, manufacturing cost can be lowered because only two output terminals are required for the DC-DC converter. Moreover, since the resistors R1 to R6 are provided in the outside of the DC-DC converter (hybrid IC), these resistors can be exchanged easily. Therefore, the voltages V HCOM, V HSEG, V M, V LSEG, V LCOM can be

adjusted easily.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 250612-82-9P

AΒ

(prepn. of peptide derivs. for the imaging of angiogenic disorders) RN 250612-82-9 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate)
(9CI) (CA INDEX NAME)

CM 1

CRN 250612-81-8 CMF C87 H137 N23 O23

PAGE 2-A

СН2-СО2Н

CM 2

CRN 76-05-1 CMF C2 H F3 O2

F-C-CO₂H

IT 250612-06-7P 250612-07-8P

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250612-06-7 USPATFULL CN Cyclo(L-arginylglycyl-1

Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

RN 250612-07-8 USPATFULL

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM . 1

CRN 250612-06-7 CMF C75 H113 N23 O23

PAGE 1-A

PAGE 1-B

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250614-38-1P 250614-39-2P 250614-40-5P

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250614-38-1 USPATFULL,

CN Yttrate(2-)-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-B

PAGE 2-A

$$(CH2)3$$

$$R2$$

$$NH2$$

$$NH2$$

●2 H+

RN 250614-39-2 USPATFULL

CN Lutetate(2-)-177Lu, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
O & R2 \\
\hline
N & O & H \\
N & N & N \\
H & O & N \\
O & Ph & CO2^{-}
\end{array}$$

PAGE 2-A

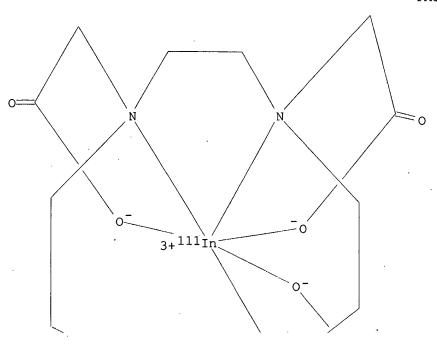
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R2 NH

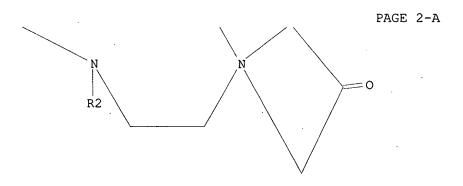
●2 H+

RN 250614-40-5 USPATFULL

CN Indate(2-)-111In, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N1
0]acetyl]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-Dphenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-A





R2

PAGE 4-A

●2 H+

X

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=> d 152 bib abs hitrn 13 14
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L52 ANSWER 13 OF 14 USPAT2

AN 2002:321986 USPAT2

TI Vitronectin receptor antagonist pharmaceuticals

IN Harris, Thomas D., Salem, NH, United States

Rajopadhye, Milind, Westford, MA, United States

PA Bristol-Myers Squibb Pharma Company, Princeton, NJ, United States (U.S.

corporation)

PI US 6511648 B2 20030128

AI US 1999-465300 19991217 (9)

PRAI US 1998-112732P 19981218 (60)

DT Utility

FS GRANTED

EXNAM Primary Examiner: Jones, Dameron L.

LREP O'Brien, Maureen P., Dolan, Peter L., Golian, Paul D.

CLMN Number of Claims: 125

ECL Exemplary Claim: 1

DRWN 0 Drawing Figure(s); 0 Drawing Page(s)

LN.CNT 8733

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention describes novel compounds of the formula:

(Q).sub.d--L.sub.n--C.sub.h,

useful for the diagnosis and treatment of cancer, methods of imaging tumors in a patient, and methods of treating cancer in a patient. The present invention also provides novel compounds useful for monitoring therapeutic angiogenesis treatment and destruction of new angiogenic vasculature. The present invention further provides novel compounds useful for imaging atherosclerosis, restenosis, cardiac ischemia, and myocardial reperfusion injury. The present invention still further provides novel compounds useful for the treatment of rheumatoid arthritis. The pharmaceuticals are comprised of a targeting moiety that binds to a receptor that is upregulated during angiogenesis, an optional linking group, and a therapeutically effective radioisotope or

diagnostically effective imageable moiety. The imageable moiety is a gamma ray or positron emitting radioisotope, a magnetic resonance imaging contrast agent, an X-ray contrast agent, or an ultrasound contrast agent.

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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     250612-82-9P
        (prepn. of peptide derivs. for the imaging of angiogenic disorders)
ΙT
     250612-06-7P 250612-07-8P
        (prepn. of peptide derivs. for the imaging of angiogenic disorders)
     250614-38-1P 250614-39-2P 250614-40-5P
TΨ
        (prepn. of peptide derivs. for the imaging of angiogenic disorders)
L52 ANSWER 14 OF 14 USPAT2
ΑN
       2002:26835 USPAT2
TI
       Quinolone vitronectin receptor antagonist pharmaceuticals
ΙN
       Harris, Thomas David, Salem, NH, United States
PA
       Bristol-Myers Squibb Pharma Company, Princeton, NJ, United States (U.S.
       corporation)
ΡI
       US 6524553
                          B2
                               20030225
AΙ
       US 1999-281209
                               19990330 (9)
PRAI
       US 1998-80150P
                           19980331 (60)
       US 1998-112715P
                           19981218 (60)
       US 1998-112829P
                           19981218 (60).
       US 1998-112732P
                           19981218 (60)
       US 1998-112831P
                           19981218 (60)
DT
       Utility
FS
       GRANTED
       Primary Examiner: Jones, Dameron L.
EXNAM
       O'Brien, Maureen P., Dolan, Peter L., Golian, Paul D.
CLMN
       Number of Claims: 18
ECL
       Exemplary Claim: 1
DRWN
       0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 5742
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AΒ
       The present invention describes novel compounds of the formula:
       (Q).sub.d--L.sub.n--C.sub.h,
       useful for the diagnosis and treatment of cancer, methods of imaging
       tumors in a patient, and methods of treating cancer in a patient. The
       present invention also provides novel compounds useful for monitoring
       therapeutic angiogenesis treatment and destruction of new angiogenic
       vasculature. The pharmaceuticals are comprised of a targeting moiety
       that binds to a receptor that is upregulated during angiogenesis, an
       optional linking group, and a therapeutically effective radioisotope or
       diagnostically effective imageable moiety. The imageable moiety is a
       gamma ray or positron emitting radioisotope, a magnetic resonance
       imaging contrast agent, an X-ray contrast agent, or an ultrasound
       contrast agent.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     250612-82-9P
        (prepn. of peptide derivs. for the imaging of angiogenic disorders)
IT
     250612-06-7P 250612-07-8P
        (prepn. of peptide derivs. for the imaging of angiogenic disorders)
IT
     250614-38-1P 250614-39-2P 250614-40-5P
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(prepn. of peptide derivs. for the imaging of angiogenic disorders)

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FILE COVERS 1907 - 4 Jun 2003 VOL 138 ISS 23 FILE LAST UPDATED: 3 Jun 2003 (20030603/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr tot 162

L62 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2003 AC

AN 2003:235416 HCAPLUS

DN 138:255514

TI Pharmaceuticals for the imaging of angiogenic disorders for use in combination therapy

IN Rajopadhye, Milind; Edwards, D. Scott; Barrett, John A.;
Carpenter, Alan P., Jr.; Harris, Thomas D.; Heminway, Stuart J.;
Liu, Shuang; Singh, Prahlad R.

PA Bristol-Myers Squibb Pharma Company, USA

SO U.S., 86 pp., Cont.-in-part of U.S. Ser. No. 281,474. CODEN: USXXAM

DT Patent

LA English

IC ICM A61K051-00 ICS A61M036-14

NCL 424001690; 424001110; 424001650; 424009100; 534014000

CC 34-3 (Amino Acids, Peptides, and Proteins) Section cross-reference(s): 8, 63, 78

FAN.CNT 7

11111.	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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ΡI	US 6537520	В1	20030325	US 2000-599295	20000621
	US 6322770	B1	20011127	US 1999-281207	19990330
	US 2002001566	A1	20020103	US 1999-281474	19990330
	US 2002015680	A1	20020207	US 1999-281209	19990330
•	US 6524553	В2	20030225		
•	US 6548663	В1	20030415	US 1999-281050	19990330
PRA]	US 1998-80150P	P	19980331		
	US 1998-112715P	P.	19981218		
	US 1999-281474	A2	19990330		
	US 1998-112732P	Р	19981218		
	US 1998-112829P	P	19981218	•	
	US 1998-112831P	P	19981218		
Λ¢	MADDAT 130.25551	1			

OS MARPAT 138:255514

AB Compds. (Q)d-(Ln)m-Ch (Q is a peptide, d=1-10, Ln is a linking group, m=0-1, Ch is a metal-bonding unit) were prepd. for use in the diagnosis and treatment of cancer in combination therapy in a patient. The present invention also provides novel compds. useful for monitoring therapeutic angiogenesis treatment and destruction of new angiogenic vasculature. The pharmaceuticals are comprised of a targeting moiety that binds to a

ST

IT

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TT

IT

TΨ

TΤ

TΤ

IT

ΙT

23214-92-8, Doxorubicin

Prednimustine

receptor that is upregulated during angiogenesis, an optional linking group, and a therapeutically effective radioisotope or diagnostically effective imageable moiety. Thus, cyclo(Arg-Gly-Asp-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]benzenesulfonic acid]-3-aminopropyl)-Val} was prepd. by acylation of cyclo{Arg-Gly-Asp-D-Tyr(3-aminopropyl)-Val} with 2-[[[5-[[(2,5-dioxo-1pyrrolidinyl)oxy]carbonyl]-2-pyridinyl]hydrazono]methyl]benzenesulfonic acid monosodium salt and converted into radiopharmaceutical 99mTc(VnA)(tricine)(phosphine), where VnA represents the vitronectin receptor antagonist. cyclic peptide radiolabeled prepn imaging angiogenic disorder; radiopharmaceutical cyclic peptide prepn vitronectin receptor antagonist anticancer agent Imaging agents (NMR contrast; prepn. of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy) Interferons Interleukin 2 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (anticancer agents as adjuvants in the treatment of cancer with peptide derivs. and their radioactive metal complexes) Peptides, preparation RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (cyclic; prepn. of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy) Angiogenesis Antitumor agents Human Radiopharmaceuticals (prepn. of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy) Vitronectin receptors RL: BSU (Biological study, unclassified); BIOL (Biological study) (prepn. of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy) Radiosensitizers, biological (radiosensitizers as adjuvants in the treatment of cancer with peptide derivs. and their radioactive metal complexes) Neoplasm Rheumatoid arthritis (treatment of; prepn. of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy) Integrins RL: BSU (Biological study, unclassified); BIOL (Biological study) (.alpha.v.beta.3, disease assocd. with; prepn. of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy) 50-07-7, Mitomycin 57-22-7, Vincristine 57-83-0, Progesterone, biological studies 59-05-2, Methotrexate 125-84-8, Aminoglutethimide 302-79-4, Tretinoin 147-94-4, Cytarabine 434-07-1, Oxymetholone 566-48-3, Formestane 488-41-5, Mitobronitol 2363-58-8, Epitiostanol 3094-09-5, Doxifluridine 3778-73-2, Ifosfamide 4291-63-8, Cladribine 4759-48-2, Isotretinoin 4533-39-5, Nitracrine 6620-60-6, Proglumide 9034-40-6, Lhrf 9014-02-2, Zinostatin 9050-67-3, Sizofilan 10318-26-0, Mitolactol 10540-29-1, Tamoxifen 13311-84-7, Flutamide 13425-98-4, Improsulfan 14769-73-4, Levamisole 17902-23-7, Tegafur 18016-80-3, Lisuride 18883-66-4, Streptozocin 20830-81-3, Daunorubicin 21416-67-1, Razoxane 21362-69-6, Mepitiostane 22181-94-8, Butocin

24279-91-2, Carboquone

39325-01-4, Picibanil 41575-94-4, Carboplatin 42471-28-3, Nimustine

29767-20-2, Teniposide

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33419-42-0, Etoposide

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     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (prepn. of peptide derivs. for the imaging of angiogenic disorders and
        the treatment of cancer in combination therapy)
TT
     108-30-5, reactions
                           288-88-0, 1H-1,2,4-Triazole
                                                          5437-45-6, Benzyl
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     Diethylenetriaminepentaacetic dianhydride
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        (prepn. of peptide derivs. for the imaging of angiogenic disorders and
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        (prepn. of peptide derivs. for the imaging of angiogenic disorders and
        the treatment of cancer in combination therapy)
     22541-90-8, reactions
IT
     RL: RGT (Reagent); RACT (Reactant or reagent)
        (prepn. of peptide derivs. for the imaging of angiogenic disorders and
        the treatment of cancer in combination therapy)
     250614-59-6P
IT
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (prepn. of peptide derivs. for the imaging of angiogenic disorders and
        the treatment of cancer in combination therapy)
ΙT
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               7091-44-3
                           250612-27-2
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (prepn. of peptide derivs. for the imaging of angiogenic disorders and
        the treatment of cancer in combination therapy)
IT
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               14269-78-4, Yb169, biological studies
                                                       14378-26-8, Re188,
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     Ir192, biological studies
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                                                       15766-00-4, Sm153,
    biological studies
                         15840-01-4, Dy166, biological studies
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ΙT
     22668-01-5
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        (radiosensitizers as adjuvants in the treatment of cancer with peptide
        derivs. and their radioactive metal complexes)
RE.CNT
      110
             THERE ARE 110 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.
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P71P

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- 250612-06-7P 250612-07-8P IT

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

RN 250612-06-7 HCAPLUS

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1yl]acetyl]-L-glutamoyl]bis- (9CI) (CA INDEX NAME)

RN 250612-07-8 HCAPLUS

CN Cyclo(L-arginylglycyl-L-alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-06-7 CMF C75 H113 N23 O23

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250614-38-1P 250614-39-2P 250614-40-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

RN 250614-38-1 HCAPLUS

CN Yttrate(2-)-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]-1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N10] acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

PAGE 2-A

RN 250614-39-2 HCAPLUS

CN Lutetate(2-)-177Lu, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]-1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N10] acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-B

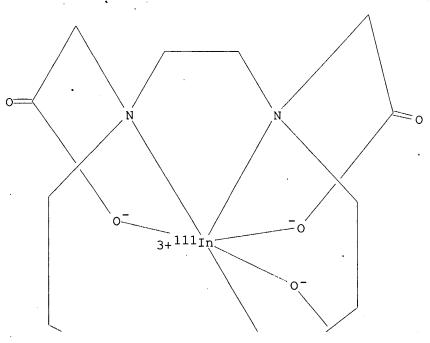
PAGE 2-A

$$(CH_2)$$
 $\stackrel{H}{\stackrel{N}{\stackrel{N}{\longrightarrow}}}$ NH_2 $R2$ NH

●2 H+

RN 250614-40-5 HCAPLUS CN Indate(2-)-111In, [[

Indate(2-)-111In, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N10]
acetyl]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-Dphenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)



R2

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 4-A

2 H+

IT 250612-82-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

RN 250612-82-9 HCAPLUS

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-81-8 CMF C87.H137 N23 O23

PAGE 2-A

| СН₂— СО₂Н

CM 2

CRN 76-05-1 CMF C2 H F3 O2

F-C-CO₂H

IT 10098-91-6, y90, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (radioisotope for use with peptide derivs. for the treatment of cancer in combination therapy)

RN 10098-91-6 HCAPLUS

CN Yttrium, isotope of mass 90 (8CI, 9CI) (CA INDEX NAME)

90_Y

L62 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2003 ACS

AN 2002:595337 HCAPLUS

DN 137:140780

TI Simultaneous imaging of cardiac perfusion and a vitronectin receptor

targeted imaging agent

IN Carpenter, Alan P.

PA USA

SO U.S. Pat. Appl. Publ., 86 pp. CODEN: USXXCO

DT Patent

LA English

IC A61M036-14; A61K051-00

NCL 424001690

CC 34-3 (Amino Acids, Peptides, and Proteins) Section cross-reference(s): 8, 63, 78

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡĪ	US 2002106325	A1	20020808	US 2001-995388	20011127
PRAI	PH 2000-7201	Α	20001127	•	•

OS MARPAT 137:140780

The invention describes a method of concurrent imaging in a mammal comprising: (a) administering a vitronectin receptor targeted imaging agent and a perfusion imaging agent, (b) concurrently detecting the vitronectin target imaging agent bound at the vitronectin receptor and the perfusion imaging agent, and (c) forming an image from the detection of the vitronectin receptor targeted imaging agent and the perfusion imaging agent. Compds. claimed include those of formula (Q)d-Ln-Ch, where Q is a peptide, d is 1-10, Ln is a linking group, and Ch is a metal bonding unit. Thus, cyclo[Arg-Gly-Asp-D-Tyr[N-[2-[[[5-(carbonyl)-2-pyridinyl]hydrazono]methyl]benzenesulfonic acid]-3-aminopropyl]-Val] was prepd. and applied to the synthesis of complex 99mTc(VnA)(tricine)(TPPTS), where VnA represents the vitronectin receptor antagonist and TPPTS is P(m-C6H4SO3Na)3.

ST peptide radiopharmaceutical prepn cardiac perfusion vitronectin receptor imaging agent

IT Perfusion

(heart; prepn. of peptides and simultaneous imaging of cardiac perfusion and a vitronectin receptor targeted imaging agent)

IT Heart

(perfusion; prepn. of peptides and simultaneous imaging of cardiac perfusion and a vitronectin receptor targeted imaging agent)

IT Angiogenesis

Imaging agents

Radiopharmaceuticals

(prepn. of peptides and simultaneous imaging of cardiac perfusion and a vitronectin receptor targeted imaging agent)

IT Vitronectin receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (prepn. of peptides and simultaneous imaging of cardiac perfusion and a vitronectin receptor targeted imaging agent)

IT Peptides, preparation

RL: DGN (Diagnostic use); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of peptides and simultaneous imaging of cardiac perfusion and a vitronectin receptor targeted imaging agent)

IT Imaging

(tumor; prepn. of peptides and simultaneous imaging of cardiac perfusion and a vitronectin receptor targeted imaging agent)

IT 288-88-0DP, 1H-1,2,4-Triazole, technetium-99m cyclopeptide tricine complexes 5704-04-1DP, Tricine, technetium-99m cyclopeptide triazole complexes 14133-76-7DP, cyclopeptide tricine triazole complexes, preparation

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

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                                                  250611-99-5P
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     250612-03-4P
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     RL: DGN (Diagnostic use); RCT (Reactant); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT
     (Reactant or reagent); USES (Uses)
        (prepn. of peptides and simultaneous imaging of cardiac perfusion and a
        vitronectin receptor targeted imaging agent)
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               250612-23-8DP, technetium-99m tricine triazole complex
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                    250612-25-0P
                                   250612-26-1P
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        (prepn. of peptides and simultaneous imaging of cardiac perfusion and a
        vitronectin receptor targeted imaging agent)
IT
    13966-01-3, biological studies
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    127455-27-0, Technetium-99 tetrofosmin
                                              131410-48-5, Gadodiamide
    131608-78-1, 99MTcN-NOET
                                142481-95-6, Technetium Tc 99m furifosmin
    193901-90-5, Gadofosveset trisodium
    RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);
    USES (Uses)
        (prepn. of peptides and simultaneous imaging of cardiac perfusion and a
        vitronectin receptor targeted imaging agent)
TΤ
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           5437-45-6, Benzyl bromoacetate
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    RL: RCT (Reactant); RACT (Reactant or reagent)
        (prepn. of peptides and simultaneous imaging of cardiac perfusion and a
        vitronectin receptor targeted imaging agent)
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    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. of peptides and simultaneous imaging of cardiac perfusion and a
        vitronectin receptor targeted imaging agent)
IT
     250612-07-8P
     RL: DGN (Diagnostic use); RCT (Reactant); SPN (Synthetic preparation); THU
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(Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT

(Reactant or reagent); USES (Uses)

(prepn. of peptides and simultaneous imaging of cardiac perfusion and a vitronectin receptor targeted imaging agent)

RN 250612-07-8 HCAPLUS

Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CN

CRN 250612-06-7

CMF C75 H113 N23 O23

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250614-38-1P 250614-39-2P 250614-40-5P

RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of peptides and simultaneous imaging of cardiac perfusion and a vitronectin receptor targeted imaging agent)

RN 250614-38-1 HCAPLUS

CN Yttrate(2-)-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]-1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N10] acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-A

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PAGE 2-A

RN

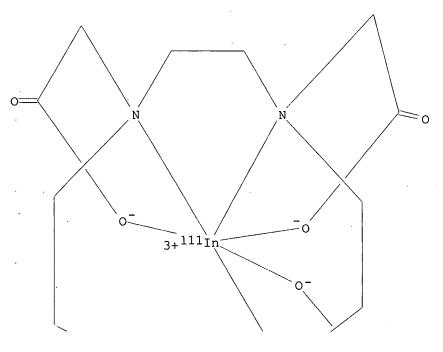
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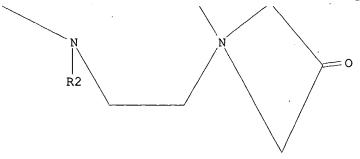
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PAGE 2-A

●2 H+

RN 250614-40-5 HCAPLUS
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acetyl]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-Dphenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)





R2

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 4-A

2 H+

IT 250612-82-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of peptides and simultaneous imaging of cardiac perfusion and a vitronectin receptor targeted imaging agent)

RN 250612-82-9 HCAPLUS

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-81-8 CMF C87 H137 N23 O23

PAGE 2-A

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CM 2

CRN 76-05-1 CMF C2 H F3 O2

L62 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2003 ACS

AN 2002:539558 HCAPLUS

DN 137:109487

TI Simultaneous imaging of cardiac perfusion and a vitronectin receptor targeted imaging agent

IN Carpenter, Alan P., Jr.

PA Bristol-Myers Squibb Medical Imaging, Inc., USA

SO PCT Int. Appl., 272 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K051-00

CC 34-3 (Amino Acids, Peptides, and Proteins) Section cross-reference(s): 8, 63, 78

FAN.CNT 1

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APPLICATION NO.
     PATENT NO.
                      KIND DATE
                                                            DATE
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PRAI US 2000-253324P
                       Ρ
OS
     MARPAT 137:109487
AB ·
     The invention describes a method of concurrent imaging in a mammal
     comprising: (a) administering a vitronectin receptor targeted imaging
     agent and a perfusion imaging agent, (b) concurrently detecting the
     vitronectin target imaging agent bound at the vitronectin receptor and the
     perfusion imaging agent, and (c) forming an image from the detection of
     the vitronectin receptor targeted imaging agent and the perfusion imaging
            Compds. claimed include those of formula (Q)d-Ln-Ch, where Q is a
     peptide, d is 1-10, Ln is a linking group, and Ch is a metal bonding unit.
     Thus, cyclo[Arg-Gly-Asp-D-Tyr[N-[2-[[[5-(carbonyl)-2-
     pyridinyl]hydrazono]methyl]benzenesulfonic acid]-3-aminopropyl]-Val] was
     prepd. and applied to the synthesis of complex 99mTc(VnA) (tricine) (TPPTS),
     where VnA represents the vitronectin receptor antagonist and TPPTS is
     P(m-C6H4SO3Na)3.
ST
     peptide radiopharmaceutical prepn cardiac perfusion vitronectin receptor
     imaging agent
IT
     Perfusion
        (heart; prepn. of peptides and simultaneous imaging of cardiac
        perfusion and a vitronectin receptor targeted imaging agent)
IT
     Heart
        (perfusion; prepn. of peptides and simultaneous imaging of cardiac
        perfusion and a vitronectin receptor targeted imaging agent)
IT
     Angiogenesis
     Imaging agents
     Radiopharmaceuticals
        (prepn. of peptides and simultaneous imaging of cardiac perfusion and a
        vitronectin receptor targeted imaging agent)
IT
     Vitronectin receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (prepn. of peptides and simultaneous imaging of cardiac perfusion and a
        vitronectin receptor targeted imaging agent)
IT
     Peptides, preparation
     RL: DGN (Diagnostic use); RCT (Reactant); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT
     (Reactant or reagent); USES (Uses)
        (prepn. of peptides and simultaneous imaging of cardiac perfusion and a
        vitronectin receptor targeted imaging agent)
IT
     Imaging
        (tumor; prepn. of peptides and simultaneous imaging of cardiac
        perfusion and a vitronectin receptor targeted imaging agent)
IT
     288-88-0DP, 1H-1,2,4-Triazole, technetium-99m cyclopeptide tricine
                 5704-04-1DP, Tricine, technetium-99m cyclopeptide triazole
               14133-76-7DP, cyclopeptide tricine triazole complexes,
     complexes
     preparation
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (prepn. of peptide derivs. for the imaging of angiogenic disorders)
IT
     250611-73-5P
                    250611-75-7P
                                   250611-77-9P 250611-79-1P
                                                                 250611-81-5P
     250611-83-7P
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250611-87-1P 250611-89-3P

250611-91-7P

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250611~93-9P
                    250611-95-1P
                                   250611-97-3P
                                                   250611-99-5P
                                                                  250612-01-2P
     250612-03-4P
                    250612-05-6P 250612-07-8P
                                                 250612-08-9P
     250612-09-0P
                    250612-11-4P
     RL: DGN (Diagnostic use); RCT (Reactant); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT
     (Reactant or reagent); USES (Uses)
        (prepn. of peptides and simultaneous imaging of cardiac perfusion and a
        vitronectin receptor targeted imaging agent)
ΙT
                7091-44-3P
                             250611-72-4DP, technetium-99m tricine triazole
     63-89-8P
     complex
               250612-23-8DP, technetium-99m tricine triazole complex
     250612-24-9P
                    250612-25-0P
                                   250612-26-1P
                                                   250612-27-2P
                                                                  250614-19-8P
                    250614-21-2P
                                   250614-22-3P
     250614-20-1P
                                                   250614-23-4P
                                                                  250614-24-5P
     250614-25-6P
                    250614-26-7P
                                   250614-27-8P
                                                   250614-28-9P
                                                                  250614-29-0P
                                                   250614-33-6P
     250614-30-3P
                    250614-31-4P
                                   250614-32-5P
                                                                  250614-34-7P
     250614-35-8P
                    250614-36-9P
                                   250614-37-0P 250614-38-1P
                                 250614-41-6P
                                                 250614-42-7P
     250614-39-2P 250614-40-5P
     250614-43-8P
                    250614-44-9P
                                   250614-45-0P
                                                   250614-46-1P
                                                                  250614-47-2P
     250614-48-3P
                    250614-49-4P
                                   250614-50-7P
                                                   250614-51-8P
                                                                  250614-52-9P
     250614-53-0P
                    250614-54-1P
                                   250614-55-2P
                                                   250614-56-3P
                                                                  250614-57-4P
     250614-58-5P
                    250614-59-6P
                                   443125-64-2P
                                                   443125-65-3P
                                                                  443125-66-4P
     443125-67-5P
                    443125-68-6P
                                   443125-69-7P
                                                   443125-71-1P
     RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic
     use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (prepn. of peptides and simultaneous imaging of cardiac perfusion and a
        vitronectin receptor targeted imaging agent)
ΙT
     13966-01-3, biological studies
                                      80529-93-7, Gadopentetic acid
     109581-73-9, Technetium Tc 99m sestamibi
                                                 120066-54-8, Gadoteridol
     127455-27-0, Technetium-99 tetrofosmin
                                              131410-48-5, Gadodiamide
     131608-78-1, 99MTcN-NOET
                                142481-95-6, Technetium Tc 99m furifosmin
     193901-90-5, Gadofosveset trisodium
     RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);
     USES (Uses)
        (prepn. of peptides and simultaneous imaging of cardiac perfusion and a
        vitronectin receptor targeted imaging agent)
ΙT
     67-43-6, Diethylenetriaminepentaacetic acid
                                                   108-30-5, Succinic
     anhydride, reactions
                                                           3674-06-4, Boc phe
                            288-88-0, 1H-1,2,4-Triazole
           5437-45-6, Benzyl bromoacetate
                                           5704-04-1, Tricine
                                                                  63995-70-0,
     Tppts
             63995-75-5, Tppms
                                 64018-22-0, Tppds
                                                      122555-91-3
                                              250612-84-1D, resin-bound
     194920-62-2
                   250612-83-0D, resin-bound
                   250612-87-4
     250612-85-2
                                 250612-88-5D, resin-bound
                                                              250612-89-6D,
     resin-bound
                   250612-90-9D, resin-bound
                                               250612-92-1D, resin-bound
     250612-93-2D, resin-bound
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (prepn. of peptides and simultaneous imaging of cardiac perfusion and a
        vitronectin receptor targeted imaging agent)
IT
     137076-54-1P
                    192635-89-5P
                                   246234-73-1P
                                                   250612-28-3P
                                                                  250612-30-7P
     250612-31-8P
                    250612-32-9P
                                   250612-34-1P
                                                   250612-36-3P
                                                                  250612-38-5P
     250612-40-9P
                    250612-41-0P
                                   250612-42-1P
                                                   250612-43-2P
                                                                  250612-44-3P
     250612-46-5P
                    250612-48-7P
                                   250612-50-1P
                                                   250612-51-2P
                                                                  250612-52-3P
     250612-54-5P
                    250612-56-7P
                                   250612-57-8P
                                                   250612-59-0P
                                                                  250612-61-4P
     250612-62-5P
                    250612-64-7P
                                   250612-65-8P
                                                   250612-67-0P
                                                                  250612-69-2P
     250612-71-6P
                    250612-72-7P
                                   250612-74-9P
                                                   250612-75-0P
                                                                  250612-77-2P
     250612-78-3P
                    250612-80-7P 250612-82-9P
                                                 250612-86-3P
     250612-94-3P
                    250636-75-0P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent) .
        (prepn. of peptides and simultaneous imaging of cardiac perfusion and a
        vitronectin receptor targeted imaging agent)
TΤ
     250612-07-8P
     RL: DGN (Diagnostic use); RCT (Reactant); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT
```

(prepn. of peptides and simultaneous imaging of cardiac perfusion and a

(Reactant or reagent); USES (Uses)

vitronectin receptor targeted imaging agent)

RN 250612-07-8 HCAPLUS

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-06-7 CMF C75 H113 N23 O23

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CM 2

CRN 76-05-1. CMF C2 H F3 O2

IT 250614-38-1P 250614-39-2P 250614-40-5P

RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of peptides and simultaneous imaging of cardiac perfusion and a vitronectin receptor targeted imaging agent)

RN 250614-38-1 HCAPLUS

CN Yttrate(2-)-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]-1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N10] acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-B

PAGE 2-A

●2 H+

RN 250614-39-2 HCAPLUS

CN Lutetate(2-)-177Lu, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]-1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N10] acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

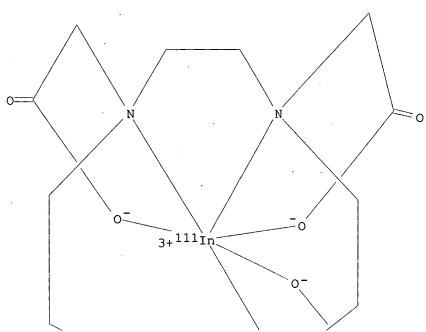
PAGE 1-B

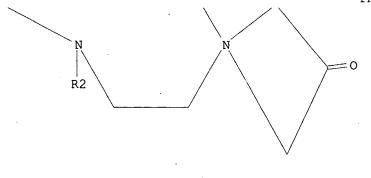
PAGE 2-A

RN 250614-40-5 HCAPLUS

CN Indate(2-)-111In, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]-1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N10] acetyl]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-A





R2

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 4-A

2 H+

IT 250612-82-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of peptides and simultaneous imaging of cardiac perfusion and a vitronectin receptor targeted imaging agent)

RN 250612-82-9 HCAPLUS

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-81-8 CMF C87 H137 N23 O23

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PAGE 2-A

CM 2

CRN 76-05-1 CMF C2 H F3 O2

L62 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2003 ACS

AN 2002:51305 HCAPLUS

DN 136:123597

TI Preparation of stable radiopharmaceutical compositions useful for tumor therapy

IN Liu, Shuang; Barrett, John A.; Carpenter, Alan
P., Jr.

PA Dupont Pharmaceuticals Company, USA

SO PCT Int. Appl., 127 pp. CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K051-04 ICS A61K051-08

CC 63-5 (Pharmaceuticals)

sharareh - 09 / 899629 Section cross-reference(s): 8, 34, 78 FAN.CNT 1 KIND DATE APPLICATION NO. DATE PATENT NO. ______ A2 . WO 2001-US21261 20010705 WO 2002004030 20020117 PΙ A3 20030227 WO 2002004030 AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG US 2002122768 20020905 US 2001-899629 20010705 Α1 20030521 EP 2001-984147 20010705 EP 1311301 A2 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR PRAI US 2000-216396P Ρ 20000706 WO 2001-US21261 W 20010705 OS MARPAT 136:123597 AΒ The present invention provides stable radiopharmaceutical compns. including a therapeutic radionuclide and an effective stabilizing amt. of an arom. stabilizer (e.g., a polyhydroxylated arom. compd., an arom. amine, or a hydroxylated arom. amine), alone or in combination with other antioxidants or stabilizers, to inhibit radiolytic degrdn. of radiopharmaceuticals. The present invention also provides improved radiopharmaceutical formulations by the use of an arom. stabilizing agent (e.g., a polyhydroxylated arom. compd., an arom. amines, or a hydroxylated arom. amine), and/or low temp. storage. The present invention also provides processes for making stable radiopharmaceutical compns. The present invention also provides the use of the pharmaceutical compns. in medical therapy and/or medical diagnosis. ST radiopharmaceutical stabilization gentisate hydroxybenzoate; sulfonatobenzeneamine ascorbate radiopharmaceutical stabilization; antioxidant hydroxybenzaldehyde radiopharmaceutical stabilization; radionuclide chelator biomol conjugate prepn stabilization TΤ Carcinoma (adenocarcinoma; stabilized radiopharmaceutical compns. for use in medical therapy and/or medical diagnosis) ΙT Uterus, neoplasm (cervix; stabilized radiopharmaceutical compns. for use in medical therapy and/or medical diagnosis) ΙΤ Interferons Interleukin 2 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (chemotherapeutic agent; prepn. of stable radiopharmaceutical compns. useful for tumor therapy) ΙT Intestine, neoplasm (colon; stabilized radiopharmaceutical compns. for use in medical therapy and/or medical diagnosis) ΙT Intestine, neoplasm (colorectal; stabilized radiopharmaceutical compns. for use in medical therapy and/or medical diagnosis) ΙT Radionuclides, biological studies.

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (complexes, radionuclides; prepn. of stable radiopharmaceutical compns.
 useful for tumor therapy)
Radiology
 (diagnostic; stabilized radiopharmaceutical compns. for use in medical
 therapy and/or medical diagnosis)
Angiogenesis

ΙT

IT

```
(disease assocd. with receptors in; stabilized radiopharmaceutical
        compns. for use in medical therapy and/or medical diagnosis)
     Epidermal growth factor receptors
ΙT
     Fibrinogen receptors
     Growth factor receptors
     Integrins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (disease assocd. with; stabilized radiopharmaceutical compns. for use
        in medical therapy and/or medical diagnosis)
TT
     Uterus, neoplasm
        (endometrium; stabilized radiopharmaceutical compns. for use in medical
        therapy and/or medical diagnosis)
TΥ
        (glioma; stabilized radiopharmaceutical compns. for use in medical
        therapy and/or medical diagnosis)
TΤ
     Selectins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ligands, disease assocd. with; stabilized radiopharmaceutical compns.
        for use in medical therapy and/or medical diagnosis)
ΤТ
     Antibodies
    .RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);
    USES (Uses)
        (monoclonal, labeled; prepn. of stable radiopharmaceutical compns.
        useful for tumor therapy)
ТΤ
     Biliary tract
     Bladder
     Esophagus
     Larynx
     Mammary gland
     Prostate gland
        (neoplasm; stabilized radiopharmaceutical compns. for use in medical
        therapy and/or medical diagnosis)
IT
     Nerve, neoplasm
        (neuroblastoma; stabilized radiopharmaceutical compns. for use in
        medical therapy and/or medical diagnosis)
IT
     Salivary gland
        (parotid, cancer; stabilized radiopharmaceutical compns. for use in
        medical therapy and/or medical diagnosis)
IT
     Peptides, biological studies
     RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
     USES (Uses)
        (prepn. of chelator-optional linker-biomol. conjugates for use in
        stable radiopharmaceutical compns.)
IΤ
    Antitumor agents
     Drug delivery systems
     Imaging agents
     Radiopharmaceuticals
     Stabilizing agents
        (prepn. of stable radiopharmaceutical compns. useful for tumor therapy)
TΤ
     Ligands
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (selectin, disease assocd. with; stabilized radiopharmaceutical compns.
        for use in medical therapy and/or medical diagnosis)
IT
     Lung, neoplasm
        (small-cell carcinoma; stabilized radiopharmaceutical compns. for use
        in medical therapy and/or medical diagnosis)
ΙT
     Carcinoma
        (squamous cell; stabilized radiopharmaceutical compns. for use in
        medical therapy and/or medical diagnosis)
IT Animal tissue
     Atherosclerosis
     Drug delivery systems
```

Heart, disease Infection Inflammation Kidney, disease Kidney, neoplasm Liver, neoplasm Lung, neoplasm Melanoma Organ, animal Ovary, neoplasm Pancreas, neoplasm Radiosensitizers, biological Stomach, neoplasm Testis, neoplasm Thyroid gland, neoplasm Transplant rejection Uterus, neoplasm (stabilized radiopharmaceutical compns. for use in medical therapy and/or medical diagnosis) Androgen receptors RL: BSU (Biological study, unclassified); BIOL (Biological study) (stabilized radiopharmaceutical compns. for use in medical therapy and/or medical diagnosis) Embolism (thromboembolism; stabilized radiopharmaceutical compns. for use in medical therapy and/or medical diagnosis) Interferons RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (.alpha., chemotherapeutic agent; prepn. of stable radiopharmaceutical compns. useful for tumor therapy) Integrins RL: BSU (Biological study, unclassified); BIOL (Biological study) (.alpha.IIb.beta.3, disease assocd. with; stabilized radiopharmaceutical compns. for use in medical therapy and/or medical diagnosis) Integrins Integrins RL: BSU (Biological study, unclassified); BIOL (Biological study) (.alpha.v.beta.3, disease assocd. with; stabilized radiopharmaceutical compns. for use in medical therapy and/or medical diagnosis) Integrins RL: BSU (Biological study, unclassified); BIOL (Biological study) (.alpha.v.beta.5, disease assocd. with; stabilized radiopharmaceutical compns. for use in medical therapy and/or medical diagnosis) RL: BSU (Biological study, unclassified); BIOL (Biological study) (.alpha.1.beta.1, disease assocd. with; stabilized radiopharmaceutical compns. for use in medical therapy and/or medical diagnosis) Integrins RL: BSU (Biological study, unclassified); BIOL (Biological study) (.alpha.4.beta.1, disease assocd. with; stabilized radiopharmaceutical compns. for use in medical therapy and/or medical diagnosis) Integrins Integrins RL: BSU (Biological study, unclassified); BIOL (Biological study) (.alpha.5.beta.1, disease assocd. with; stabilized radiopharmaceutical compns. for use in medical therapy and/or medical diagnosis) Interferons RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (.beta., chemotherapeutic agent; prepn. of stable radiopharmaceutical compns. useful for tumor therapy) Interferons

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

TΤ

IT.

IΤ

IT

ΙT

TT.

IT

IT

TT

IT

IT

```
(.gamma., chemotherapeutic agent; prepn. of stable radiopharmaceutical
       compns. useful for tumor therapy)
ΙT
                          57-22-7, Vincristine
    50-07-7, Mitomycin
                                                 57-83-0, Progesterone,
    biological studies
                          59-05-2, Methotrexate
                                                125-84-8, Aminoglutethimide
    147-94-4, Cytarabine
                           302-79-4, Tretinoin
                                                  434-07-1, Oxymetholone
     488-41-5, Mitobronitol
                             566-48-3, Formestane
                                                     2363-58-8, Epitiostanol
    3094-09-5, Doxifluridine
                                3778-73-2, Ifosfamide
                                                        4291-63-8, Cladribine
                            4759-48-2, Isotretinoin
     4533-39-5, Nitracrine
                                                       6620-60-6, Proglumide
                                               9050-67-3, Sizofilan
    9014-02-2, Zinostatin
                             9034-40-6, Lhrf
    10318-26-0, Mitolactol
                             10540-29-1, Tamoxifen
                                                      13311-84-7, Flutamide
    13425-98-4, Improsulfan
                              14769-73-4, Levamisole
                                                       17902-23-7, Tegafur
    18016-80-3, Lisuride
                          18883-66-4, Streptozocin
                                                       20830-81-3, Daunorubicin
    21362-69-6, Mepitiostane
                               21416-67-1, Razoxane
                                                       22181-94-8, Butocin
    23214-92-8, Doxorubicin
                              24279-91-2, Carboquone
                                                       29069-24-7,
    Prednimustine
                     29767-20-2, Teniposide
                                             33419-42-0, Etoposide
    39325-01-4, Picibanil
                            41575-94-4, Carboplatin
                                                       42471-28-3, Nimustine
    51264-14-3, Amsacrine
                             53643-48-4, Vindesine
                                                   53910-25-1, Pentostatin
    54350-48-0, Etretinate
                            55726-47-1, Enocitabine
                                                        58337-35-2, Elliptinium
               61422-45-5, Carmofur
                                    62304-98-7, Thymalfasin 71486-22-1,
                   74050-98-9, Ketanserin 81627-83-0, Colony stimulating
               81840-15-5, Vesnarinone 83869-56-1, Colonystimulating
    factor-1
     factor-2
               90357-06-5, Bicalutamide
                                         92118-27-9, Fotemustine
    95058-81-4, Gemcitabine
                              95734-82-0, Nedaplatin
                                                        98631-95-9, Sobuzoxane
    102676-47-1, Fadrozole 112809-51-5, Letrozole
                                                       112887-68-0, Raltitrexed
    120287-85-6, Cetrorelix
                             173146-27-5, Denileukin diftitox
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (chemotherapeutic agent; prepn. of stable radiopharmaceutical compns.
       useful for tumor therapy)
IT
    80449-02-1, Tyrosine kinase
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (disease assocd. with; stabilized radiopharmaceutical compns. for use
       in medical therapy and/or medical diagnosis)
IT
    108-68-9
               769-39-1
                          2419-94-5
                                       2969-81-5
                                                   6066-82-6
                                                               18807-71-1
    114559-25-0
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                                 208580-27-2
                                              277316-35-5
                                                             277316-57-1
    RL: RCT (Reactant); RACT (Reactant or reagent)
        (prepn. of chelator-optional linker-biomol. conjugates for use in
       stable radiopharmaceutical compns.)
ΙT
    40324-66-1P
                  57932-18-0P
                                 161552-03-0P
                                                246234-73-1P
                                                               250612-43-2P
                   250612-48-7P 250612-82-9P
    250612-45-4P
                                                277315-71-6P
    277315-82-9P
                   277315-89-6P
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                                                  277316-24-2P
                                                                 .277316-27-5P
    277316-28-6P
                   277316-29-7P
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                                                  277316-31-1P
                                                                 277316-40-2P
    277316-41-3P
                   277316-44-6P
                                   277316-45-7P
                                                  277316-58-2P
                                                                 389885-48-7DP,
    oxime resin-bound
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. of chelator-optional linker-biomol. conjugates for use in
       stable radiopharmaceutical compns.)
ΙT
                   277315-68-1P
                                   277315-72-7P
    RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
    BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
    USES (Uses)
        (prepn. of chelator-optional linker-biomol. conjugates for use in
        stable radiopharmaceutical compns.)
IΤ
                   278173-02-7P
                                   278173-08-3P
                                                  390798-27-3P
    RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic
    use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (prepn. of stable radiopharmaceutical compns. useful for tumor therapy)
ΙT
    10043-66-0D, Iodine 131, complexes, biological studies 10098-91-6D
     , 90Y, complexes, biological studies
                                           13967-65-2D, Holmium 166,
    complexes, biological studies
                                     13981-25-4D, Copper 64, complexes,
    biological studies
                         13981-27-6D, Zirconium 89, complexes, biological
               13981-59-4D, Tin 117, complexes, biological studies
    13982-06-4D, Copper 60, complexes, biological studies
                                                             14119-09-6D,
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```
Gallium 67, complexes, biological studies
                                            14133-76-7D, 99Tc, complexes,
biological studies
                     14158-31-7D, Iodine 125, complexes, biological
         14265-75-9D, 177Lu, complexes, biological studies
                                                              14276-53-0D.
Copper 62, complexes, biological studies
                                           14378-26-8D, Rhenium 188,
complexes, biological studies
                                14391-96-9D, Scandium 47, complexes,
biological studies
                     14596-37-3D, Phosphorus 32, complexes, biological
         14687-25-3D, Lead 203, complexes, biological studies
14913-89-4D, complexes, biological studies
                                             14981-64-7D, Palladium 109,
complexes, biological studies
                               14998-63-1D, Rhenium 186, complexes,
                     15715-08-9D, Iodine 123, complexes, biological
biological studies
         15750-15-9D, Indium 111, complexes, biological studies
15755-39-2D, Astatine 211, complexes, biological studies
                                                           15757-14-9D,
                                           15757-86-5D, Copper 67,
Gallium 68, complexes, biological studies
complexes, biological studies
                               15758-35-7D, Ruthenium 97, complexes,
                     15765-31-8D, Promethium 149, complexes, biological
biological studies
studies
          15766-00-4D, Samarium 153, complexes, biological studies
RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
   (prepn. of stable radiopharmaceutical compns. useful for tumor therapy)
16434-14-3, Lutetium-177 trichloride 39271-65-3, Yttrium-90 trichloride
RL: RCT (Reactant); RACT (Reactant or reagent)
   (prepn. of stable radiopharmaceutical compns. useful for tumor therapy)
             27314-97-2
22668-01-5
                          70132-50-2
                                       88876-88-4
                                                    104958-90-9
108001-60-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
   (radiosensitizer agent; prepn. of stable radiopharmaceutical compns.
   useful for tumor therapy)
50-81-7, Ascorbic acid, biological studies
                                             51-85-4, Cystamine
                                                                  57-55-6,
Propylene glycol, biological studies 59-67-6, Nicotinic acid, biological
studies
         87-89-8, Inositol 89-57-6, 5-Amino-2-hydroxybenzoic acid
98-92-0, Nicotinamide
                        100-51-6, Benzyl alcohol, biological studies
134-03-2, Sodium ascorbate
                                      149-91-7, biological studies
                            137-51-9
150-13-0, p-Aminobenzoic acid 490-79-9, Gentisic
       495-08-9, Gentisyl alcohol
acid
                                  610-02-6
                                               2374-03-0
4955-90-2, Sodium gentisate
                              9004-54-0, Dextran, biological studies
13677-79-7
             389885-49-8
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
   (stabilizing agent; prepn. of stable radiopharmaceutical compns. useful
   for tumor therapy)
250612-82-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
  (prepn. of chelator-optional linker-biomol. conjugates for use in
   stable radiopharmaceutical compns.)
250612-82-9 HCAPLUS
Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[(4,7,10-tris(2-(1,1-dimethylethoxy)-2-oxoethyl)-1,4,7,10-
tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate)
     (CA INDEX NAME)
CM
     1
CRN
    250612-81-8
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TΤ

ΙT

TΤ

TΤ

RN

CN

CMF

C87 H137 N23 O23

PAGE 1-A

PAGE 1-B

PAGE 2-A

| Сн₂— со₂н CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250612-07-8P

RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of chelator-optional linker-biomol. conjugates for use in stable radiopharmaceutical compns.)

RN 250612-07-8 HCAPLUS

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-06-7 CMF C75 H113 N23 O23

PAGE 1-A

PAGE 1-B

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250614-38-1P

RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of stable radiopharmaceutical compns. useful for tumor therapy) 250614-38-1 HCAPLUS

RN 250614-38-1 HCAPLUS
CN Yttrate(2-)-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N10]
acetyl-.kappa.0]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartylD-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

PAGE 2-A

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ΙT
     10098-91-6D, 90Y, complexes, biological studies
     RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);
     USES (Uses)
        (prepn. of stable radiopharmaceutical compns. useful for tumor therapy)
     10098-91-6 HCAPLUS
RN
     Yttrium, isotope of mass 90 (8CI, 9CI) (CA INDEX NAME)
CN
90<sub>Y</sub>
     490-79-9, Gentisic acid
IT
     RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (stabilizing agent; prepn. of stable radiopharmaceutical compns. useful
        for tumor therapy)
RN
     490-79-9 HCAPLUS
     Benzoic acid, 2,5-dihydroxy- (9CI) (CA INDEX NAME)
CN
  OH
       CO<sub>2</sub>H
  OH
L62
     ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2003 ACS
     2001:935452 HCAPLUS
ΑN
     136:70083
DN
     Pharmaceuticals for the imaging of angiogenic disorders for use in
TI
     combination therapy
IN
     Rajopadhye, Milind; Edwards, D. Scott; Barrett, John A.;
     Carpenter, Alan P., Jr.; Heminway, Stuart J.; Liu, Shuang
     ; Singh, Prahlad
PA
     Dupont Pharmaceuticals Company, USA
SO
     PCT Int. Appl., 306 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
IC
     ICM A61K051-08
CC
     34-3 (Amino Acids, Peptides, and Proteins)
     Section cross-reference(s): 8, 63, 78
FAN.CNT 1
     PATENT NO.
                      KIND
                            DATE
                                            APPLICATION NO.
                                                             DATE
     _____
                      ____
                            -----
                                            -----
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                       A2
                            20011227
                                            WO 2001-US20108 20010621
     WO 2001097860
                       А3
                            20030227
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             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
             ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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EP 1311302

A2

20030521

EP 2001-946697

20010621

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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI US 2000-213206P
                            20000621
                      Р
     WO 2001-US20108
                       W
                            20010621
OS
     MARPAT 136:70083
     Compds. (Q)d-Ln-Ch (Q is a peptide, d = 1-10, Ln is a linking group, Ch is
AΒ
     a metal-bonding unit) were prepd. for use in the diagnosis and treatment
     of cancer in combination therapy in a patient. The present invention also
     provides novel compds. useful for the treatment of rheumatoid arthritis
     (no data). Thus, cyclo{Arg-Gly-Asp-D-Tyr(N-[2-[[[5-[carbony1]-2-
     pyridinyl]hydrazono]methyl]benzenesulfonic acid]-3-aminopropyl)-Val} was
     prepd. by acylation of cyclo{Arg-Gly-Asp-D-Tyr(3-aminopropyl)-Val} with
     2-[[[5-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-2-
     pyridinyl]hydrazono]methyl]benzenesulfonic acid monosodium salt and
     converted into radiopharmaceutical 99mTc(VnA)(tricine)(phosphine), where
     VnA represents the vitronectin receptor antagonist.
ST
     cyclic peptide radiolabeled prepn imaging angiogenic disorder;
     radiopharmaceutical cyclic peptide prepn vitronectin receptor antagonist
     anticancer agent
ΙT
     Imaging agents
        (NMR contrast; prepn. of peptide derivs. for the imaging of angiogenic
        disorders and the treatment of cancer in combination therapy)
ΙT
     Interferons
     Interleukin 2
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (anticancer agents as adjuvants in the treatment of cancer with peptide
        derivs. and their radioactive metal complexes)
TT
     Peptides, preparation
     RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); RACT (Reactant or reagent); USES (Uses)
        (cyclic; prepn. of peptide derivs. for the imaging of angiogenic
        disorders and the treatment of cancer in combination therapy)
IT
     Photosensitizers (pharmaceutical)
        (photosensitizers as adjuvants in the treatment of cancer with peptide
        derivs. and their radioactive metal complexes)
TT
     Angiogenesis
     Antitumor agents
     Radiopharmaceuticals
        (prepn. of peptide derivs. for the imaging of angiogenic disorders and
        the treatment of cancer in combination therapy)
IT
     Vitronectin receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (prepn. of peptide derivs. for the imaging of angiogenic disorders and
        the treatment of cancer in combination therapy)
ΙT
     Radiosensitizers, biological
        (radiosensitizers as adjuvants in the treatment of cancer with peptide
        derivs. and their radioactive metal complexes)
TT
     Neoplasm
     Rheumatoid arthritis
        (treatment of; prepn. of peptide derivs. for the imaging of angiogenic
        disorders and the treatment of cancer in combination therapy)
                                                 57-83-0, Progesterone,
ΙT
     50-07-7, Mitomycin
                          57-22-7, Vincristine
                                                 125-84-8, Aminoglutethimide
     biological studies
                          59-05-2, Methotrexate
     147-94-4, Cytarabine
                            302-79-4, Tretinoin
                                                 434-07-1, Oxymetholone
     488-41-5, Mitobronitol
                              566-48-3, Formestane
                                                    2363-58-8, Epitiostanol
                                                        4291-63-8, Cladribine
     3094-09-5, Doxifluridine
                                3778-73-2, Ifosfamide
                                                       6620-60-6, Proglumide
     4533-39-5, Nitracrine
                             4759-48-2, Isotretinoin
     9014-02-2, Zinostatin
                             9034-40-6, Lhrf
                                               9050-67-3, Sizofilan
     10318-26-0, Mitolactol
                             10540-29-1, Tamoxifen
                                                      13311-84-7, Flutamide
                               14769-73-4, Levamisole 17902-23-7, Tegafur
     13425-98-4, Improsulfan
                           18883-66-4, Streptozocin
     18016-80-3, Lisuride
                                                       20830-81-3, Daunorubicin
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21416-67-1, Razoxane

22181-94-8, Butocin

21362-69-6, Mepitiostane

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23214-92-8, Doxorubicin
                               24279-91-2, Carboquone
                                                        29069-24-7,
                   29767-20-2, Teniposide
                                             33419-42-0, Etoposide
     Prednimustine
                           41575-94-4, Carboplatin 42471-28-3, Nimustine
     39325-01-4, Picibanil
     51264-14-3, Amsacrine
                             53643-48-4, Vindesine 53910-25-1, Pentostatin
                              55726-47-1, Enocitabine
     54350-48-0, Etretinate
                                                       58337-35-2, Elliptinium
                                     62304-98-7, Thymalfasin
               61422-45-5, Carmofur
                                                               71486-22-1,
     acetate
                   74050-98-9, Ketanserin
                                            81627-83-0, Colony stimulating
     Vinorelbine
                                          83869-56-1, Colony stimulating
                81840-15-5, Vesnarinone
     factor-1
                90357-06-5, Bicalutamide
                                           92118-27-9, Fotemustine
     factor-2
     95058-81-4, Gemcitabine
                              95734-82-0, Nedaplatin
                                                        98631-95-9, Sobuzoxane
     102676-47-1, Fadrozole
                              104958-90-9 108001-60-1
                                                          112809-51-5,
                112887-68-0, Raltitrexed
                                          120287-85-6, Cetrorelix
     Letrozole
     173146-27-5, Denileukin diftitox
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (anticancer agents as adjuvants in the treatment of cancer with peptide
        derivs. and their radioactive metal complexes)
     22668-01-5
                  27314-97-2, 3-Amino-1,2,4-benzotriazine-1,4-dioxide
IT
                             70132-50-2 88876-88-4
                                                       220264-81-3
     68335-15-9, Photofrin
                   381733-54-6
                                 381733-55-7
                                               381733-56-8
                                                             381733-57-9
     220264-83-5
     381733-58-0
                   381733-59-1
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (photosensitizers as adjuvants in the treatment of cancer with peptide
        derivs. and their radioactive metal complexes)
ΙT
     202930-91-4P
                    250611-72-4P
                                   250611-73-5P
                                                  250611-74-6P
                                                                 250611-75-7P
     250611-76-8P
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                                   250611-78-0P
                                                  250611-79-1P
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                                                                 250611-85-9P
     250611-86-0P
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                                                                 250612-05-6P
     250612-06-7P 250612-07-8P
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                                                250612-09-0P
     250612-10-3P
                    250612-11-4P
     RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); RACT (Reactant or reagent); USES (Uses)
        (prepn. of peptide derivs. for the imaging of angiogenic disorders and
        the treatment of cancer in combination therapy)
IT
     250611-72-4DP, technetium-99m tricine triazole complex
                                                              250612-12-5P
                    250612-14-7P
                                                  250612-16-9P
     250612-13-6P
                                   250612-15-8P
                                                                 250612-17-0P
     250612-18-1P
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                                   250612-20-5P
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     250612-24-9P
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                                   250612-26-1P
                                                  250614-19-8P
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     250614-21-2P
                    250614-22-3P
                                   250614-23-4P
                                                  250614-24-5P
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     250614-26-7P
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                                   250614-28-9P
                                                  250614-29-0P
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                    250614-32-5P
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                                   250614-33-6P
                                                  250614-34-7P
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     250614-36-9P
                    250614-37-0P 250614-38-1P 250614-39-2P
     250614-40-5P
                    250614-41-6P
                                   250614-42-7P
                                                  250614-43-8P
    250614-44-9P
                    250614-45-0P
                                   250614-46-1P
                                                  250614-47-2P
                                                                 250614-48-3P
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (prepn. of peptide derivs. for the imaging of angiogenic disorders and
        the treatment of cancer in combination therapy)
TΤ
     108-30-5, reactions
                           288-88-0, 1H-1,2,4-Triazole
                                                         5437-45-6, Benzyl
    bromoacetate
                    5704-04-1, Tricine
                                         23911-26-4,
     Diethylenetriaminepentaacetic dianhydride
                                                 63995-70-0, Tppts
                         64018-22-0, TPPDS
     63995-75-5, TPPMS
                                             122555-91-3
                                                           161552-03-0
                   186305-11-3
                                 194920-62-2
     180468-25-1
                                               250612-83-0D, resin-bound
                                 250612-85-2D, resin-bound
     250612-84-1D, resin-bound
                                                             250612-86-3
     250612-87-4
                   250612-88-5D, resin-bound 250612-89-6D, resin-bound
     250612-90-9D, resin-bound
                                 250612-92-1D, resin-bound
                                                             250612-93-2D,
     resin-bound
                   250612-94-3
     RL: RCT (Reactant); RACT (Reactant or reagent)
       (prepn. of peptide derivs. for the imaging of angiogenic disorders and
```

```
the treatment of cancer in combination therapy)
TΤ
    137076-54-1P
                    192635-89-5P
                                   246234-73-1P
                                                  250612-28-3P
                                                                 250612-30-7P
     250612-31-8P
                                   250612-34-1P
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                    250612-32-9P
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     250612-40-9P
                    250612-41-0P
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                    250612-48-7P
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     250612-46-5P
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                    250612-56-7P
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                                                                 250612-61-4P
                    250612-64-7P
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     250612-62-5P
                                                                 250612-69-2P
                    250612-72-7P
                                   250612-74-9P
                                                  250612-75-0P
                                                                 250612-77-2P
     250612-71-6P
                    250612-80-7P 250612-82-9P
                                                250636-75-0P
     250612-78-3P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. of peptide derivs. for the imaging of angiogenic disorders and
        the treatment of cancer in combination therapy)
IT
     22541-90-8, reactions
     RL: RGT (Reagent); RACT (Reactant or reagent)
        (prepn. of peptide derivs. for the imaging of angiogenic disorders and
        the treatment of cancer in combination therapy)
ΙT
     250614-59-6P
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (prepn. of peptide derivs. for the imaging of angiogenic disorders and
        the treatment of cancer in combination therapy)
ΙT
     63-89-8
               7091-44-3
                           250612-27-2
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (prepn. of peptide derivs. for the imaging of angiogenic disorders and
        the treatment of cancer in combination therapy)
ΙT
     10098-91-6, y90, biological studies
                                           13967-64-1, Dy165,
     biological studies 13967-65-2, Ho166, biological studies
     La140, biological studies
                                 14041-42-0, Gd159, biological studies
     14041-44-2, Yb175, biological studies 14158-31-7, i125, biological
                                                      14378-26-8, Re188,
               14269-78-4, Yb169, biological studies
     biological studies
                         14391-11-8, Au199, biological studies
     Ir192, biological studies
                                14913-49-6, Bi212, biological studies
     14913-89-4, Rh105, biological studies 14914-12-6, Lu 174, biological
                                                       14981-64-7, Pd109,
               14967-68-1, Pd103, biological studies
                         14998-63-1, Re186, biological studies 15749-66-3,
     biological studies
     p33, biological studies
                               15756-45-3, Au192, biological studies
     15757-86-5, Cu67, biological studies 15760-04-0, Ag111, biological
               15765-31-8, Pm149, biological studies
                                                       15766-00-4, Sm153,
                        15840-01-4, Dy166, biological studies
     biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (radioisotope for use with peptide derivs. for the treatment of cancer
        in combination therapy)
ΙT
     250612-06-7P 250612-07-8P
     RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); RACT (Reactant or reagent); USES (Uses)
        (prepn. of peptide derivs. for the imaging of angiogenic disorders and
        the treatment of cancer in combination therapy)
RN
     250612-06-7 HCAPLUS
CN
     Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl),
     5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-
     yl]acetyl]-L-glutamoyl]bis- (9CI) (CA INDEX NAME)
```

PAGE 1-A

PAGE 1-B

RN 250612-07-8 HCAPLUS CN Cyclo(L-arginylglycyl-L-

Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-06-7

CMF C75 H113 N23 O23

PAGE 1-A

PAGE 1-B

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250614-38-1P 250614-39-2P 250614-40-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

RN 250614-38-1 HCAPLUS

CN Yttrate(2-)-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]-1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N10] acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-B

PAGE 2-A

$$(CH2)3$$

$$H$$

$$NH2$$

$$NH$$

$$R2$$

$$NH$$

●2 H+

RN 250614-39-2 HCAPLUS

CN Lutetate(2-)-177Lu, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]-1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N10] acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

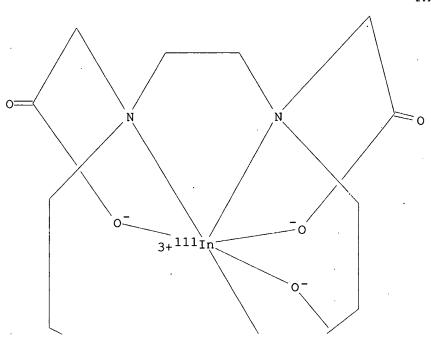
PAGE 2-A

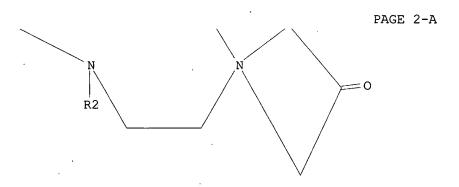
●2 H+

RN 250614-40-5 HCAPLUS

CN Indate(2-)-111In, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]-1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N10] acetyl]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-A





R2

PAGE 4-A

●2 H+

IT 250612-82-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

RN 250612-82-9 HCAPLUS

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 25.0612-81-8

CMF C87 H137 N23 O23

PAGE 1-A

PAGE 1-B

PAGE 2-A

CM 2

CRN 76-05-1 CMF C2 H F3 O2

F-C-CO₂H

IT 10098-91-6, y90, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (radioisotope for use with peptide derivs. for the treatment of cancer in combination therapy)

RN 10098-91-6 HCAPLUS

CN Yttrium, isotope of mass 90 (8CI, 9CI) (CA INDEX NAME)

90_Y

L62 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2003 ACS

AN 2001:421741 HCAPLUS

DN 135:177368

TI 90Y and 177Lu Labeling of a DOTA-Conjugated Vitronectin Receptor Antagonist Useful for Tumor Therapy

AU Liu, Shuang; Cheung, Eric; Ziegler, Marisa C.; Rajopadhye, Milind; Edwards, D. Scott

CS Medical Imaging Division, **DuPont** Pharmaceuticals Company, North Billerica, MA, 01862, USA

SO Bioconjugate Chemistry (2001), 12(4), 559-568 CODEN: BCCHES; ISSN: 1043-1802

PB American Chemical Society

DT Journal

LA English

CC 8-9 (Radiation Biochemistry)

The 90Y and 177Lu complexes (RP697 and RP688, resp.) of a AB DOTA-conjugated vitronectin receptor antagonist (SU015: 2-(1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)-1-cyclododecyl)acetyl-Glu(cyclo{Lys-Arg-Gly-Asp-D-Phe})-cyclo{Lys-Arg-Gly-Asp-D-Phe}) were prepd. by reacting SU015 with the radiometal chloride in ammonium acetate buffer (pH > 7.2) in the presence of an antioxidant (sodium gentisate, GA). Through a series of radiolabeling expts., it was found that there are many factors influencing the rate of 90Y chelation and the radiolabeling efficiency of SU015. These include the purity of SU015, the pH, reaction temp., and heating time, as well as the presence of trace metal contaminants, such as Ca2+, Fe3+, and Zn2+. The chelation of 90Y by SU015 is slow, so that heating at elevated temps. (50-100 .degree.C) is needed to complete the 90Y-labeling. The rate of 90Y chelation is also dependent on the pH of the reaction mixt. Under optimized radiolabeling conditions (pH 7.2-7.8 and heating at 50-100 .degree.C for 5-10 min), the min. amt. of SU015 required to achieve 95% RCP for RP697 is .apprx.25 .mu.g for 20 mCi of 90YCl3 corresponding to a SU015:90Y ratio of .apprx.30:1.

ST yttrium lutetium labeling DOTA conjugate vitronectin receptor antitumor

IT Vitronectin receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (antagonist; 90Y and 177Lu labeling of DOTA-conjugated vitronectin receptor antagonist useful for tumor therapy)

```
IT
     Antitumor agents
     Chelation
        (90Y and 177Lu labeling of DOTA-conjugated vitronectin receptor
        antagonist useful for tumor therapy)
IT
     14127-61-8, Ca2+, uses
                              20074-52-6, Fe3+, uses
                                                       23713-49-7, Zn2+, uses
     RL: MOA (Modifier or additive use); USES (Uses)
        (contaminant; 90Y and 177Lu labeling of DOTA-conjugated vitronectin
        receptor antagonist useful for tumor therapy)
     250614-38-1P 250614-39-2P
IT
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (90Y and 177Lu labeling of DOTA-conjugated vitronectin receptor
        antagonist useful for tumor therapy)
ΙT
     4955-90-2, Sodium gentisate 16434-14-3, 177Lutetium chloride
     39271-65-3, 90Yttrium chloride
                                     94790-37-1, Hbtu
                                                         137076-54-1
     250612-70-5
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (90Y and 177Lu labeling of DOTA-conjugated vitronectin receptor
        antagonist useful for tumor therapy)
ΙT
     250612-06-7P 250612-81-8P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (90Y and 177Lu labeling of DOTA-conjugated vitronectin receptor
        antagonist useful for tumor therapy)
ΙT
     60239-18-1DP, Dota, vitronectin receptor antagonist conjugated with,
     radiolabeled
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (90Y and 177Lu labeling of DOTA-conjugated vitronectin receptor
        antagonist useful for tumor therapy)
RE.CNT
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- IT 250614-38-1P 250614-39-2P
 - RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (90Y and 177Lu labeling of DOTA-conjugated vitronectin receptor antagonist useful for tumor therapy)
- RN 250614-38-1 HCAPLUS
- CN Yttrate(2-)-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]-1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N10] acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

PAGE 2-A

RN 250614-39-2 HCAPLUS

CN Lutetate(2-)-177Lu, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N10]
acetyl-.kappa.0]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartylD-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

PAGE 2-A

●2 H⁺

IT 250612-06-7P 250612-81-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(90Y and 177Lu labeling of DOTA-conjugated vitronectin receptor antagonist useful for tumor therapy)

RN 250612-06-7 HCAPLUS

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis- (9CI) (CA INDEX NAME)

PAGE 1-A

RN 250612-81-8 HCAPLUS
CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis- (9CI) (CA INDEX NAME)

O t-BuO-C-CH₂
t-BuO-C-CH₂
N
O
CH₂
CH₂
CH₂
CH₂

PAGE 2-A

СН2-СО2Н

L62 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2003 ACS

AN 2001:421740 HCAPLUS

DN 135:185318

TI Stabilization of 90Y-Labeled DOTA-Biomolecule Conjugates Using Gentisic Acid and Ascorbic Acid

AU Liu, Shuang; Edwards, D. Scott

CS Medical Imaging Division, **DuPont** Pharmaceuticals Company, North Billerica, MA, 01862, USA

SO Bioconjugate Chemistry (2001), 12(4), 554-558 CODEN: BCCHES; ISSN: 1043-1802

PB American Chemical Society

DT Journal

LA English

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 34, 78

AB Radiolytic degrdn. of radiolabeled compds. is a major challenge for the development of new therapeutic radiopharmaceuticals. The goal of this study is to explore the factors influencing the soln. stability of a 90Y-labeled DOTA-peptide conjugate (RP697), including the amt. of total activity, the activity concn., the stabilizer concn., and the storage temp. In general, the rate of radiolytic decompn. of RP697 is much slower at the lower activity concn. (<4 mCi/mL) than that at the higher concn. (>10 mCi/mL). RP697 remains relatively stable at the 20 mCi level and room temp. while it decomps. rapidly at the 100 mCi level under the same storage conditions. Radical scavengers, such as gentisic acid (GA) and ascorbic acid (AA), were used in combination with the low temp. (-78 .degree.C) to prevent the radiolytic decompn. of RP697. It was found that RP697 remains stable for at least 2 half-lives of 90Y when GA or AA (10 mg for

20 mCi of 90Y) is used as a stabilizer when the radiopharmaceutical compn. is stored at -78 .degree.C. The stabilizer (GA and AA) can be added into the formulation either before or after radiolabeling. The post-labeling approach is particularly useful when the use of a large amt. of the stabilizer interferes with the radiolabeling. The radiopharmaceutical compn. developed in this study can also apply to other 90Y-labeled DOTA-biomol. conjugates. The amt. of the stabilizer used in the radiopharmaceutical compn. and storage temp. should be adjusted according to the sensitivity of the radiolabeled DOTA-biomol. conjugate toward radiolytic decompn.

ST DOTA peptide conjugate stabilization Y90 labeled; yttrium90 DOTA peptide conjugate stabilization; radiolysis Y90 DOTA peptide conjugate stabilization

IT Radiolysis

Stabilizing agents

(stabilization of 90Y-labeled DOTA-biomol. conjugates using gentisic acid and ascorbic acid)

IT 250614-38-1P

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (stabilization of 90Y-labeled DOTA-biomol. conjugates using

gentisic acid and ascorbic acid)

IT 134-03-2, Sodium ascorbate 4955-90-2, Sodium gentisate
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)

(stabilization of 90Y-labeled DOTA-biomol. conjugates using gentisic acid and ascorbic acid)

IT 39271-65-3, yttrium 90 chloride **250612-06-7**

RL: RCT (Reactant); RACT (Reactant or reagent) (stabilization of 90Y-labeled DOTA-biomol. conjugates using gentisic acid and ascorbic acid)

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

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IT 250614-38-1P

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (stabilization of 90Y-labeled DOTA-biomol. conjugates using gentisic acid and ascorbic acid)

RN 250614-38-1 HCAPLUS

CN Yttrate(2-)-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]-1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N10] acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 1-B

PAGE 2-A

●2 H⁺

IT 250612-06-7

RL: RCT (Reactant); RACT (Reactant or reagent) (stabilization of 90Y-labeled DOTA-biomol. conjugates using gentisic acid and ascorbic acid)

RN 250612-06-7 HCAPLUS

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis- (9CI) (CA INDEX NAME)

US 6524553

US 6548663

PRAI US 1998-80150P

NO 2000004917

US 1998-112715P

В2

B1

Α

P

Ρ

20030415

20001102

19980331

19981218

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ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2003 ACS
L62
     1999:736515 HCAPLUS
ΑN
DN
     131:351678
ΤI
     Preparation of peptide derivatives for the imaging of angiogenic disorders
     Rajopadhye, Miland; Edwards, D. Scott; Harris, Thomas D.; Heminway, Stuart
ΙN
     J.; Liu, Shuang; Singh, Prahlad R.
PA
     Du Pont Pharmaceuticals Company, USA
SO
     PCT Int. Appl., 213 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
     ICM A61K049-00
IC
CC
     34-3 (Amino Acids, Peptides, and Proteins)
     Section cross-reference(s): 8; 78
FAN.CNT 7
     PATENT NO.
                      KIND
                            DATE
                                            APPLICATION NO.
                                                              DATE
PI
     WO 9958162
                       A2
                             19991118
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MARPAT 131:351678
Compds. (Q)d-Ln-Ch (Q is a peptide, d= 1-10, Ln is a linking group, Ch is
a metal-bonding unit) were prepd. for use in the diagnosis and treatment
of cancer, methods of imaging tumors in a patient, and methods of treating
cancer in a patient. The present invention also provides novel compds.
useful for monitoring therapeutic angiogenesis treatment and destruction
of new angiogenic vasculature. Thus, cyclo{Arg-Gly-Asp-D-Tyr(N-[2-[[[5-
[carbonyl]-2-pyridinyl]hydrazono]methyl]benzenesulfonic
acid]-3-aminopropyl)-Val} was prepd. by acylation of cyclo{Arg-Gly-Asp-D-
Tyr (3-aminopropy1)-Val with 2-[[[5-[(2,5-dioxo-1-
pyrrolidinyl)oxy]carbonyl]-2-pyridinyl]hydrazono]methyl]benzenesulfonic
acid monosodium salt and converted into radiopharmaceutical
99mTc(VnA)(tricine)(phosphine), where VnA represents the vitronectin
receptor antagonist.
cyclic peptide radiolabeled prepn imaging angiogenic disorder
Imaging
   (NMR; prepn. of peptide derivs. for the imaging of angiogenic
   disorders)
Peptides, preparation
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
USES (Uses)
   (cyclic; prepn. of peptide derivs. for the imaging of angiogenic
   disorders)
Blood vessel
   (formation; prepn. of peptide derivs. for the imaging of angiogenic
   disorders)
Angiogenesis
Antitumor agents
Imaging
Rheumatoid arthritis
Scintigraphy
Tomography
   (prepn. of peptide derivs. for the imaging of angiogenic disorders)
Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
   (prepn. of peptide derivs. for the imaging of angiogenic disorders)
                                                    5437-45-6, Benzyl
108-30-5, reactions
                     288-88-0, 1H-1,2,4-Triazole
               5704-04-1, Tricine
bromoacetate
                                    23911-26-4,
                                            63995-70-0, Tppts
Diethylenetriaminepentaacetic dianhydride
                                        122555-91-3
63995-75-5, TPPMS
                    64018-22-0, TPPDS
                                                      161552-03-0
                            194920-62-2
180468-25-1
              186305-11-3
                                          250612-83-0D, resin-bound
250612-84-1D, resin-bound
                            250612-85-2D, resin-bound
                                                        250612-86-3
                                         250612-89-6D, resin-bound
              250612-88-5D, resin-bound
250612-87-4
                            250612-92-1D, resin-bound
250612-90-9D, resin-bound
                                                        250612-93-2D,
              250612-94-3
resin-bound
RL: RCT (Reactant); RACT (Reactant or reagent)
   (prepn. of peptide derivs. for the imaging of angiogenic disorders)
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                                             250612-28-3P
                                                             250612-30-7P
                              246234-73-1P
               250612-32-9P
                                             250612-36-3P
                                                             250612-38-5P
250612-31-8P
                              250612-34-1P
250612-40-9P
               250612-41-0P
                                             250612-43-2P
                                                             250612-44-3P
                              250612-42-1P
250612-46-5P
               250612-48-7P
                              250612-50-1P
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250612-54-5P
               250612-56-7P
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                              250612-57-8P
                                                             250612-61-4P
                                             250612-67-0P
250612-62-5P
               250612-64-7P
                              250612-65-8P
                                                             250612-69-2P
               250612-72-7P
                                             250612-75-0P
250612-71-6P
                              250612-74-9P
                                                             250612-77-2P
               250612-80-7P 250612-82-9P
250612-78-3P
                                           250636-75-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
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(prepn. of peptide derivs. for the imaging of angiogenic disorders)
ΙT
     202930-91-4P
                    250611-72-4P
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     250611-76-8P
                                                   250611-79-1P
                    250611-77-9P
                                    250611-78-0P
                                                                   250611-80-4P
     250611-81-5P
                    250611-82-6P
                                    250611-83-7P
                                                   250611-84-8P
                                                                   250611-85-9P
                                                   250611-89-3P
     250611-86-0P
                    250611-87-1P
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                    250611-92-8P
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                                                   250611-94-0P
                                                                   250611-95-1P
                                    250611-98-4P
                                                   250611-99-5P
                                                                   250612-00-1P
     250611-96-2P
                    250611-97-3P
                                    250612-03-4P
                                                   250612-04-5P
                                                                   250612-05-6P
     250612-01-2P
                    250612-02-3P
                                  250612-08-9P
                                                 250612-09-0P
     250612-06-7P 250612-07-8P
     250612~10-3P
                    250612-11-4P
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     USES (Uses)
        (prepn. of peptide derivs. for the imaging of angiogenic disorders)
IT
     288-88-0DP, 1H-1,2,4-Triazole, technetium-99m cyclopeptide tricine
                 5704-04-1DP, Tricine, technetium-99m cyclopeptide triazole
                 14133-76-7DP, cyclopeptide tricine triazole complexes,
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     preparation
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                    250612-23-8DP, technetium-99m tricine triazole complex
     250612-22-7P
                    250612-25-0P
                                    250612-26-1P
                                                   250614-19-8P
                                                                   250614-20-1P
     250612-24-9P
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     250614-31-4P
                                    250614-33-6P
                                                                   250614-35-8P
                    250614-37-0P 250614-38-1P 250614-39-2P
     250614-36-9P
                                    250614-42-7P
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     250614-40-5P
                    250614-41-6P
     250614-44-9P
                    250614-45-0P
                                    250614-46-1P
                                                   250614-47-2P
                                                                   250614-48-3P
     250614-49-4P
                    250614-50-7P
                                    250614-51-8P
                                                   250614-52-9P
                                                                   250614-53-0P
                    250614-55-2P
                                    250614-56-3P
                                                   250614-57-4P
     250614-54-1P
                                                                   250614-58-5P
     250614-59-6P
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (prepn. of peptide derivs. for the imaging of angiogenic disorders)
ΙT
               7091-44-3
                           250612-27-2
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (prepn. of peptide derivs. for the imaging of angiogenic disorders)
ΙT
     250612-82-9P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. of peptide derivs. for the imaging of angiogenic disorders)
     250612-82-9 HCAPLUS
RN
CN
     Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl),
     5,5'-[N-[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10-
     tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate)
            (CA INDEX NAME)
          1
     CM
     CRN
          250612-81-8
     CMF
          C87 H137 N23 O23
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PAGE 1-B

PAGE 2-A

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250612-06-7P 250612-07-8P

RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250612-06-7 HCAPLUS

CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis- (9CI) (CA INDEX NAME)

RN 250612-07-8 HCAPLUS
CN Cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250612-06-7 CMF C75 H113 N23 O23

CM 2

CRN 76-05-1 CMF C2 H F3 O2

IT 250614-38-1P 250614-39-2P 250614-40-5P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of peptide derivs. for the imaging of angiogenic disorders)

RN 250614-38-1 HCAPLUS

CN Yttrate(2-)-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]-1,4,7,10-tetraazacyclododec-1-yl-.kappa.Ni,.kappa.N4,.kappa.N7,.kappa.N10] acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

PAGE 2-A

RN 250614-39-2 HCAPLUS

CN Lutetate(2-)-177Lu, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.O)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N10]
acetyl-.kappa.O]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartylD-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

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PAGE 1-B

PAGE 2-A

●2 H⁺

RN 250614-40-5 HCAPLUS

CN

Indate(2-)-111In, [[5,5'-[N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N10]
acetyl]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-.alpha.-aspartyl-Dphenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

R2

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

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L2
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               E US2000-216396/AP, PRN
             1 S E5
L3
             1 S L1-L3
L4
L5
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           549 S TRIHYDROXYBENZOIC ACID
L7
            30 S TRIHYDROXY BENZOIC ACID
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L9
             6 S TRI HYDROXYBENZOIC ACID
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L22
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           9 S L22 NOT (170 OR HYDROPEROXY)
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L24
            9 S L14, L23
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L26
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L28
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L35
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L38
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L39
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L40
              E KRGDF/SQEP
            138 S E3
            42 S L41 AND MULTICHAIN/NTE
L43
            28 S L42 AND 10/SQL
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             6 S L43 AND (C75H108INN23O23 OR C75H113N23O23 OR C87H137N23O23 OR
             7 S L35, L44
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